# NOBEL LAUREATES

## IN PHYSIOLOGY OR MEDICINE [1901 TO 1991]

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# *Foreword*

Since the first time the Nobel Prize was incepted in 1901, Alfred Nobel s Will has been carried out almost every year Barring unavoidable interferences like the world wars, this prize for scientific and literary excellence and world peace has brought into limelight and recognition eminent humanists and persuasive thinkers and researchers who have pioneered the shaping of the world in the past over 100 years

The members of the jury selecting the prize winners have repeatedly distinguished themselves by their professional and impartial judgement Should we wish today, after this considerable lapse of time once again to nominate the most important figures from the various scientific fields, the greater part of the list could hardly be any different—with just a few names missing and a few added

The unbiased attitude of the committee which selects the laureates in different spheres and their commitment to strictly enforce Nobel's last wishes that it is his will *That the award of the prize shall be made without regard to nationality*

*so that he who has the greatest merit, shall receive it, be he a Scandinavian or not,'* has rarely, if ever, been seriously contested

## The Will of Alfred Nobel

The Nobel Foundation was established under the terms of the will of Alfred Bernhard Nobel, Ph D h c , dated Paris, November 27, 1895, which in its relevant parts runs as follows

*The whole of my remaining realizable estate shall be dealt with in the following way the capital, invested in safe securities by my executors shall constitute a fund, the interest on which shall be annually distributed in the form of prizes to those who, during the preceding year shall have conferred the greatest benefit on mankind The said interest shall be divided into five equal parts which shall be apportioned as follows one part to the person who shall have made the most important discovery or invention within the field of physics, one part to the person who shall have made the most important chemical discovery within the domain of physiology or medicine, one part to the person who shall have produced in the field of literature the most outstanding work of an idealistic tendency, and one part to the person who shall have done the most or the best work for fraternity between nations, for the abolition or reduction of standing armies and for the holding and promotion of peace congresses The prizes for physics and chemistry shall be awarded by the Swedish Academy of Sciences, that for physiological or medical works by the Caroline Institute in Stockholm that for literature by the Academy in Stockholm and that for champions of peace by a committee of five persons to be elected by the Norwegian Storting It is my express wish that in awarding the prizes no consideration whatever shall be given to the nationality of the candidates but that the most worthy shall receive the prize whether he be a Scandinavian or not*

## The Nobel Phenomenon

Since the first award was given in 1901, the Nobel prize has always been regarded by laymen, scholars and scientists alike as the ultimate symbol of excellence in achievements The Nobelists, undoubtedly, occupy the topmost hierarchy in their area of work and are considered peers In the late 19th century when Nobel contemplated the awards, there was no substantial support for scholars or researchers As an inventor and scientist with over 350 patents under his belt, Nobel was aware that the cost of most research, though modest, were beyond an independent scientist's means For example, even as late as 1920, the research grant for the entire Cavendish Laboratory was only about 10,000 dollars or 2,000 pounds for a year One of the major prizes available at that time, the Royal Society's Rumford medal by comparison carried an honorarium of approximately $150 The first year Nobel award in 1901 was $42,000 each For the general public and the laureates themselves, Nobel's princely sum constituted a symbolic message asserting, in a way, that these people really mattered

The value of the prize has varied between $30,000 and $1 000,000 (1991 price value) over the years The division of Nobel prizes into two or three portions further diminishes its monetary value Although the purchase value (adjusted for inflation) still lags behind the original sum given in 1901 and no longer provides anything like the liberating endowment that Nobel envisaged for independent research the prestige of the award has increased incomparably in ninety one years of its evolution The extraordinarily deserving roster of recipients is the most distinctive aspect of this prize of all

The Nobel prize has so far been awarded to an exalted group of over 600 individuals and institutions Of these nearly a quarter at 153, have been awarded to those who have excelled in the field of physiology or medicine

One significant point that is striking, while understanding the Nobel phenomenon, is the tremendous influence the at mosphere provides to a scholar in science Association with laureates and apprenticeship under them involves not merely education and training as is ordinarily understood, but also the acquisition of the norms and standards, the values and attitudes as well as the knowledge, skills and behavioural patterns associated with particular statures and roles

Hans Krebs, the 1953 Nobel laureate in Physiology or Medicine and a student of the 1931 laureate Otto Warburg explains thus 'If I ask myself how it came about that one day I found myself in Stockholm, I have not the slightest doubt that I owe this good fortune to the circumstance that I had an outstanding teacher at the critical stage in my scientific career Otto Warburg set an example in the methods and quality of first rate research Without him, I am sure I would never have reached the standards which are prerequisites for being considered by the Nobel Com mittee '

As another laureate put it 'I knew the technique of research, I knew a lot of physics I had the words, the *libretto*, but not quite the music In other words, I had not been in contact with men who were deeply embedded in the tradition of physics men of high quality This was my first real contact with first rate minds at the high point of their power"

This book is a tribute to all those people, to their unstinting efforts at surpassing themselves to extend the frontiers of knowledge and learning, and to the untiring pursuit of perfection—a tradition that we seek to aspire to and establish, within our own corporate ranks

Dr Vijay Kumar Datla

*Chairman & Managing Director*

**Biological E Limited**

# *Introduction*

The dawn of the twentieth century, the year 1900 was an exciting year for life sciences The dramatic triple discovery of the work of Mendel by a Dutch, a German and an Austrian scientist and their simultaneous confirmation of his brilliant findings in 1900 had at long last satisfied one of man's oldest desires, to know how the distinctiveness and the very form of living things are passed along from parents to progeny Genetics has come a long way since then, so has man s understanding of the machines and the mechanics that makes a life tick. Cells with their intricate organelles and chemical functions providing the functional platforms for the chromosomes, DNA the genetic material synthesising proteins and continuing the propagation of life nervous system with its masterly specialisations that communicate impulses different blood groups and an extremely sophisticated immuno system that nourishes and balances the body, the enzymes and hormones that chemically conduct the show of life, the microbial world with bacteria and viruses and the fascinating mysteries of the living world have unfolded one by one in the century that was

1900 was also the year of the beginning of the Nobel Prizes The Nobel Assembly at the Karolinska Institute at Stockholm that chooses the Nobel Prize winners for Physiology or Medicine have carried out their unenviable job with deepest understanding and farsight in the past ninety years

The Nobel award in Physiology or Medicine in the first few years since its inception is indicative of the diverse areas of investigation that man was making into himself to understand him The very first award in 1901 went to Behring for discovering the diphtheria antitoxin followed by Ross in 1902 for discovering the transmittance of malaria and Finsen (1903) for treatment of diseases with concentrated light rays Pavlov was the first physiologist to get Nobel recognition (1904) and Golgi (1906) was the pioneer of many of his successors who were recognised for their contribution to the understanding of nervous tissue—Adrian and Sherrington (1932), Dale and Loewi (1936), Erlanger and Gasser (1944), Hess and Moniz (1949) Eccles, Hodgkin and Huxley (1963), Axelrod, Katz and Von Euler (1970), Sperry, Hubel and Wiesel (1981) and more recently Cohen and Levi-Montalcini (1986)

Studies on cell structure and chemistry (first award to Kossel in 1910), blood groups and immunochemistry (beginning with Landsteiner – 1930), and heredity and chromosomes (Morgan 1933) are some areas that dominated the Nobel awards for many years Chemists and more especially biochemists have actively participated in the quest for Physiology or Medicine and the 1962 recognition of Watson, Crick and Wilkins for their outstanding deduction of the double helix structure of the genetic material DNA established the dominance of molecular biology The link of Morgan s chromosomes beaded

through Beadle, Tatum and Lederberg (1958), Delbruck, Hershey and Luria (1969) are the first few of the elite list of Nobelists who changed the shape of molecular understanding of how gene functions The base that they so strongly built brought further insight into this fascinating field of research The mechanisms by which viruses affect the genes of cancer cells (1975), molecular genetics (1978), genetic regulation of the body's immune system (1980) jumping genes' (1983), immunochemistry (1984), gene action in antigen antibody reaction (1987) and genes that cause cancer (1988) are subsequent important works in this area that led to the Nobel awards

The extended period of investigation in one area and the lasting recognition that the Nobel Committee gives it is only illustrative of its untiring involvement in understanding of the essence of life Every speciality of life sciences that has contributed to the betterment of mans knowledge and welfare has received the careful and continuous attention and recognition of the Committee

The past ninety years have been exciting for life sciences and we have been able to penetrate deep into the heart of life s mystery As would be evident from the pages that follow contributions of the Nobelists in this great search has been almost total

## 1901

### VON BEHRING, EMIL ADOLF

Nationality German

b March 15 1854, Mansdorf, Prussia, now in Germany d March 31, 1917, Marburg Germany

*For his work on serum therapy, especially its application against diphtheria by which he has opened a new road in the domain of medical science and thereby placed in the hands of the physician a victorious weapon against illness and deaths*

As an assistant to Robert Koch in Berlin, Von Behring's main field of research was the struggle against diphtheria On his discovery that rats are immune to anthrax and that rat serum is able to destroy the anthrax bacillus, he injected guinea pigs with the bacilli and kept them alive by treating them with iodine trichloride On further injection with the bacillus the animals did not show any signs of the disease

By further experiments, he developed and demonstrated serum therapy, the theory that the serum of an animal that had been cured could be used for curing other animals Behring developed this technique further and as the quantitative requirements for the serum grew with increased indents from hospitals, he developed horse serum as a substitute for the limited quantity of guinea pig serum He succeeded finally in 1917, a few months before his death, in establishing a method for the immunization of human beings against diphtheria and producing the vaccine T A

## 1902

ROSS, SIR RONALD

Nationality British

*b* May 13, 1857 Almora India d September 16, 1932, London

*For his work on malaria, by which he has shown how it enters the organism and thereby has laid the foundation for successful research on this disease and methods of combating it*

During the years from 1881 to 1894, Ross served with the army in Madras and Burma In 1889 he married Rosa Bessie, daughter of Alfred Bradley Bloxam, they had two sons and two daughters He was on leave in England in 1894 when he met Patrick Manson and became interested in the cause of malaria Two years after his return to India (1897), he found traces of the malaria parasite in the anopheles mosquito and, a year later, discovered that a parasite in the blood of birds closely resembled the parasite of human malaria He realized that since this was transmitted by the anopheles, it was likely that human malaria was transmitted by the same agent

In 1899 Ross became a lecturer in the Liverpool School of Tropical Medicine and from 1902 to 1912 was a Professor His activities were now mainly concentrated on the elimination of the anopheles mosquito, as a means of preventing malaria

Ross always acknowledged his debt to Manson Although he did not work out the details of the cycle in human malaria, he definitely disproved the view that malaria was contracted from air or water and, in the latter part of his life, added materially to the knowledge of malarial epidemiology His publications include *Prevention of Malaria* (1910) and his *Memoirs* (1923)

In 1933, the Ross Institute and Hospital for Tropical Diseases was founded in his honour and he became its first Director-in Chief

## 1903

**FINSEN, NIELS RYBERG**

Nationality Danish

b December 15 1860 Thorshavn Faeroe Islands, Den mark d September 24, 1904, Copenhagen

*In recognition of his contribution to the treatment of diseases, especially lupus vulgaris, with concentrated light radiation, whereby he has opened a new avenue for medical science*

Niels Ryberg Finsen the Danish physician worked at the Institute of Light Therapy, Copenhagen His discovery that sunlight and electric rays contain properties that can be used to cure skin diseases and blemishes revolutionized treatment in these areas Finsen light takes its name from its discoverer The Finsen lamp is a high power device to emit concentrated or converged and filtered rays which

have bactericidal properties Ultraviolet sections of sunlight have strong bactericidal power

Finsen authored several books on light therapy and is considered as the founder of modern phototherapy Modern treatments like radiation and drug therapy owe a lot to Finsen's pioneering works with light therapy

## 1904

PAVLOV IVAN

Nationality Russian

b September 26 1849, Ryazam, Russia d February 27, 1936, Moscow

*In recognition of his work on the physiology of digestion through which knowledge on vital aspects of the subject has been transformed and enlarged*

Pavlov studied chemistry and physiology, receiving his doctorate in 1879 He then spent two years in Germany, studying the blood system and the physiology of digestion It was these two aspects of bodily function which interested him most, in particular, the way they were controlled by the brain

He found that if a dog was given food and simultaneously a bell was rung at several minutes' intervals, the dog eventually salivated at the sound of the bell, even if no food was present The dog's nervous system had learnt to associate the sound of the bell with food Pavlov called this behaviour the "conditioned reflex and the process of learning it 'conditioning' The conditioned reflex differs from an innate reflex such as the rapid withdrawal of a limb from a painful stimulus in that it has to be learnt A dog salivating when eating meat is exhibiting an unconditioned reflex If it salivates at the sight of meat, on the other hand, the reflex is conditioned As Pavlov demonstrated, a dog reared without ever seeing meat will show no response to it, not having learned to associate it with food

Continuing his studies into the psychology of learning, Pavlov found that learning the reflex would be hindered by interruptions The 'external inhibition , as it is now called, is similar to the need for peace and quiet when studying or learning any process He also discovered internal inhibition which occurred if, after a conditioned reflex such as response to the bell had been learned the food stopped appearing when the bell was rung The dog eventually stopped salivating The response was not forgotten but suppressed

One of Pavlov s most important discoveries in this field

was that the area of the brain responsible for this reflex is one found only in animals higher up on the evolutionary scale He thus tried to apply his theories to human behaviour in an attempt to explain psychotic and neurotic conditions He considered that psychotic people, who shut out the rest of the world, behave in that way because they associate all excitation with possible injury or threat

Pavlov's work has often been confused with brainwashing, but in fact many everyday responses are conditioned reflexes, from the blink of surprise to stopping a car at a red light

1905

KOCH, ROBERT

Nationality German

b December 11, 1843, Klausthal, Prussia, d May 27, 1910, Baden Baden

*For his investigations and discoveries in relation to tuberculosis*

Koch, the greatest of all pure bacteriologists, studied mathematics and science at Gottingen, but soon transferred to Medicine and graduated in 1866 The anthrax bacillus, had been identified as the cause for large scale mortality of cattle in France and Germany, but was still a great hazard as no progress had been made in treatment or prevention

Koch tackled this problem in his primitive laboratory Shortly before, Ferdinand Cohn had first observed the formation of spores by a bacillus Koch now found that in certain conditions, which he studied exhaustively, the anthrax bacillus forms spores that can survive on earth for years He passed anthrax bacilli, from the blood of an infected animal, from one mouse to another through twenty generations, and found that they bred true He showed conclusively that the anthrax bacillus is the cause and the only cause of anthrax, and he worked out its life-history

Koch next investigated the causes of infective diseases following wounds He showed that the injection of putrid material into animals could produce various septic diseases differing clinically In 1878 aniline dyes were first used to stain bacteria by Carl Weigert (1845-1904) Koch greatly improved Weigert s methods, and his masterly memoir on these researches was published in 1878

After he went to Berlin, Koch introduced his new methods for obtaining pure cultures, utilizing gelatin, agar-agar, and other substances as solid media This step (1881 1883) revolutionized bacteriology In 1882 he announced his greatest discovery the tubercle bacillus, and almost immediately Paul Ehrlich described his definitive method of

staining that organism In 1883 Koch was a member of the German Cholera Commission to Egypt, and there and in India he discovered the causative organism, the cholera vibrio In 1890 he announced that he had prepared form cultures of the tubercle bacillus a substance, tuberculin, which could be used for diagnosis and treatment As a pure bacteriologist Koch remains unequalled, and his techniques form the foundation of modern methods

## 1906

**GOLGI, CAMILLO**

Nationality Italian

b July 7,1843, Corteno, Italy,
d January 21 1926, Pavia

**RAMON Y CAJAL, SANTIAGO**

Nationality Spanish

b May 1, 1852, Pyrenees,
d October 18, 1934, Madrid

*In recognition of their work on the structure of the nervous system*

Golgi devised his silver impregnation method of staining nervous tissue (1873) This method revolutionized the histology of the nervous system In 1880 he first described the neurotendinous spindle ('organ of Golgi') found near the junction of a tendon with a muscle He classified nerve cells, and described that type in which the main process (axon) does not become a nerve fibre, but divides repeated ly to form an arborescence ( Golgi cells ) These researches were published in 1885 in his book on the histology of the nervous system Golgi s method of staining enabled in dividual nerve fibres to be followed through much of their course In 1898 he described a peculiar reticular formation in the cytoplasm of cells ('the Golgi apparatus )

In 1885 Golgi differentiated between the parasites of the tertian and the quartan types of malaria, and he showed that the beginning of a bout of fever was synchronous with that stage of the life-cycle of the parasite when numerous young parasites burst out of their containing erythrocytes into the blood stream In 1892 he showed that, whereas in intermittent types of malaria (tertian and quartan fever) the parasite passes through its life-cycle in the blood in the pernicious type of malaria the parasites develop mainly in the organs of the body, and especially in the brain

Golgi's work on the nervous system inspired that of Ramon Y Cajal

When Cajal graduated all stains for nervous tissue gave lit tle differentiation between the nervous elements proper and the supporting tissue (neuroglia) Tracking of

individual nerve fibres was therefore difficult In 1873 Golgi discovered his silver impregnation method of staining nervous tissue, which stained nerve cells and their fibres black, while leaving the neuroglia faintly stained

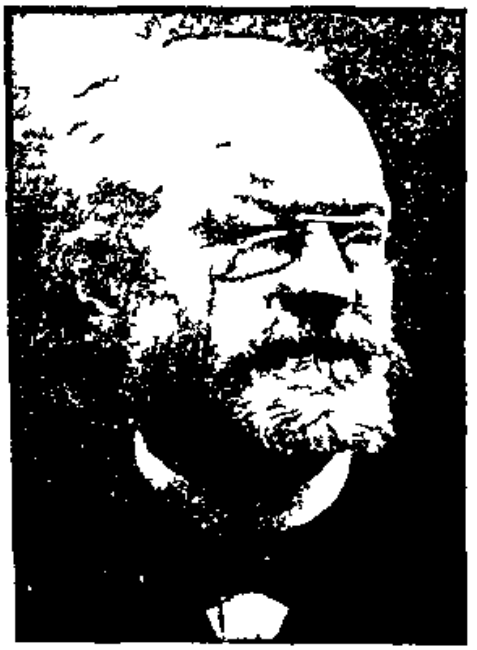
Cajal worked intensively on the histology of the grey matter, and improved Golgi's method He disproved the current theory that the grey matter is a network of anastomosing nerve fibres, and he was able to trace long nerve fibres which never fused with any others during their course He put forward the theory that fibres that appeared to join nerve cells ended in terminal buttons, which, however closely they might approach the nerve cells, never actually touched them There was thus no anatomical fusion of the substance of one nerve cell with that of another Cajal also discovered the collateral branches of the axon.

Wilhelm had suggested that the fundamental unit of the nervous system is the nerve cell with its branching processes and its axon Cajal s histological work was establishing this view when W Von Waldeyer in 1891 coined the word 'neurone' for the cell and its processes Waldeyer did no experimental or other work in this field, to which Cajal devoted the rest of his life Cajal postulated that the nerve impulse passed from the axon of one neurone to the dendrites of the next neurone, and so to its nerve cell and axon. This postulate that conduction is in one direction only, was formalized by A Van Gehuchten (1861-1914) as the law of dynamic polarity

In 1906 Cajal attacked the difficult problem of the degeneration of nerve tracts and the method of regeneration of nerve fibres after they had been cut Two opposing

solutions to the problem of regeneration had long been held, but Cajal proved that the proximal cut end of the nerve grows out to meet the degenerated distal end Cajal next turned to the neuroglia, the supporting tissue of the nerve fibres in the central nervous system, and he was able to distinguish in it three different types of cells He also studied vision in the faceted eyes of insects

## 1907



### LAVERAN, CHARLES LOUIS ALPHONSE

Nationality French

b June 18 1845 Paris d May 18 1922, Paris

*In recognition of his work on the role played by protozoa in caus ing diseases*

Laveran, the French physician, was an army surgeon in Algiers when he discovered the parasite that causes human

malaria He graduated in military medicine at Strasbourg (1867) and ind addition to his military career taught at Val de-Grace College Paris Besides his work on malaria Laveran worked on the causes of sleeping sickness (leish maniosis), and other protozoal diseases like trypanosomiasis At the Pasteur Institute, which he joined in 1897 and where he worked until his death, he estab lished the Laboratory of Tropical Diseases

## 1908

EHRLICH, PAUL

Nationality German

b March 14, 1854 Sterheln (now Stryelin in Poland), d August 20, 1915, Bad Homburg Vor Der Wohe, Germany

MECHINKOV, ILYA ILICH

Nationality Russian

b May 15, 1845, near Kharkov, Ukraine, d July 16, 1916, Paris

*In recognition of their work on immunity*

The German bacteriologist Paul Ehrlich pioneered the technique of chemotherapy in medicine From his discovery that certain tissues have a specific affinity for chemicals, he reasoned that organisms causing disease could be selectively killed with chemical drugs This led him to produce arsphenamine, the first synthetic drug, which is highly effective against syphilis

His interest in this aspect of medicine had been stimulated by reading an account of the way tissues are affected by lead It had been shown that the cells of those organs most affected during lead poisoning also absorb lead in test tube solutions That is, certain cells had an affinity for inorganic substances His work impressed the German microbiologist, Robert Koch, who offered him a post at his Institute for Infectious Diseases With a laboratory at his disposal, Ehrlich turned his attention to diphtheria

Another German physician, Emil von Behring, had shown that the toxins produced by certain bacteria such as tetanus and diphtheria stimulate the cells of the body to produce antitoxins which then neutralize the poison On the basis of these discoveries large amounts of antitoxin could be produced in animals and the serum used for therapeutic purposes Ehrlich participated in these researches and pioneered the large-scale production of diphtheria anti toxins in horses

He was particularly interested in finding a drug to cure syphilis then a prevalent and crippling disease Ehrlich read reports of the successful use of arsenic compounds against the African sleeping sickness trypanosome, an

organism resembling the syphilis spirochaete (so-called because of its spiral shape) Because arsenic compounds are generally poisonous to man, Ehrlich began to look for one which, while innocuous to man, would destroy the spirochaete In 1910, after testing over 600 compounds, Ehrlich found one which fitted the bill The name of the drug was arsphenamine and it proved to be a remarkable success Marketed under the name of 'Salvarsan' it sold all over the world and made a fortune for Ehrlich, a matter of indifference to him It also provided the starting point for the development of the synthetic drugs industry, in which the German chemical plants became leaders

Mechinkov, the Russian French biologist, was educated in Russia and Germany In Messina Italy, where he had gone on a research visit, he studied the transparent larvae of starfish and noticed that some of their cells could engulf and digest foreign particles These cell eaters he called phagocytes Furthering his work on phagocytic action at the Paris Pasteur Institute, he found that in human blood a large proportion of the leucocytes (white cells) are phagocytic and attack invading bacteria This in turn results in increased numbers of leucocytes in the infected areas followed by the inflamed area becoming hot, red, swollen and painful due to dead phagocytes forming pus

The last two decades of his life were spent on the study of human aging since he believed that phagocytes eventually begin to digest the host cells aided by the effects of intestinal bacteria and that effectively combating them would significantly increase the normal human life span

*In recognition of their work on immunity*

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## 1909

### KOCHER, EMIL THEODOR

Nationality Swiss

b August 25, 1841, Berne Switzerland d July 27, 1917, Berne

*For his work on the physiology pathology and surgery of the thyroid gland*

Kocher made innumerible contributions to techniques in a wide range of surgical operations such as those on the lungs the stomach and the gall bladder Especially important was his pioneering of ovariotomy and the application of the antiseptic surgery of Joseph Lister His surgical success also depended a great deal on the many improvements he made in appliances and instruments

Kocher's most celebrated work, however were his studies

on the thyroid gland His studies arose out of his operations — of which he performed over 5,000 during his career — for removing the thyroid Prior to Kocher, this operation had frequently been fatal, but his application of Lister's antiseptic surgery brought him great success

In 1883 Kocher announced that the complete removal of the thyroid gland led to a characteristic disease pattern but that, where a portion of the gland had been left and had grown, the disease pattern was modified The disease symptoms described by Kocher (operative myxoedema) were recognized as being analogous to those of the naturally occurring myxoedema, and Kocher's work did a great deal to co-ordinate and relate studies on malfunctions of the thyroid For instance, the fact became significant that for centuries there had been descriptions of cretinism, a form of idiocy and dwarfism, accompanied by the general symptoms of myxoedema

Kocher also made other important observations, such as the fact that hypothyroidism also resulted from such conditions as goitre He gave a tremendous general stimulus to studies on the thyroid, particularly in the search for therapeutic treatment This led to the introduction of such valuable drugs as thyroid and thyroxin

His surgical skill made a marked impact on his contemporaries particularly of course, his many students and assistants Further, Kocher published numerous studies including a celebrated *Textbook of Operative Surgery* which was translated into many languages

## 1910

### KOSSEL, ALBRECHT

Nationality German

b September 6 1853, Rostock d July 5, 1927, Heidelberg

*In recognition of the contributions to our knowledge of cell chemistry made through his work on proteins, including the nucleic substances*

A biochemist, Kossel was one of the pioneers who worked for the recognition of biochemistry as an important course material for University students as it has created an independent sphere of its own, touching on the fundamental principles of biology' Kossel came from Rostock in the North German countryside and studied medicine at the University of Strasbourg Even the Nobel Committee which gave him the award did not foresee how significant his work on the four basic elements of nucleic acids —

guamine, adenine, thymine and cytosin — was to prove for the foundation of molecular biology These four basic elements — nitrogenous bases — along with uracil, are the alphabets of the genetic code, the language of the genes

## 1911

### GULLSTRAND, ALVAR

Nationality Swedish

b June 5, 1862, Landskrona, Sweden, d July 28, 1930 Stockholm

*For his work on the dioptrics of the eye*

Gullstrand, the Swedish ophthalmologist, studied at the Universities of Uppsala, Vienna and Stockholm As a Professor of Ophthalmology at Uppsala, he was the first scientist to apply the methods of physical mathematics to the study of optical images and of the refraction of light in

the eye He worked on astigmatism, improved the ophth moscope and invented corrective lenses for use af removal of a cataract from the eye The Gullstrand s lamp, a valuable diagnostic tool for the detailed study the eye, was devised by him

Gullstrand published several papers on dioptrics (deali with the refraction of light in the eye)

## 1912

CARREL, ALEXIS

Nationality American

b June 28 1873 Lyons, France d November 5, 19 Paris

*In recognition of his work on vascular suture and the transpla tation of blood vessels and organs*

Earlier attempts to transplant organs (in order to replace diseased organs or amputated limbs etc) had failed through among other reasons, the lack of method for re-establishing a normal blood circulation through the transplanted organs An invariable cause of failure was the development of thrombosis or stenosis

Carrel, who began studying the anastomosing of vessels in 1902, systematically analysed all possible complications and developed techniques to overcome these causes of failure for example the enforcement of rigid asepsis and careful attention to details about the use of instruments, needles and suturing

Using his new techniques, he was able to remove entire organs such as the kidney and to replace them in their original location or, occasionally, in different parts of the body where they still functioned His studies were far-reaching and paved the way for innumerable advances in vascular surgery His techniques also found application in transfusing blood from donor to recipient, a technique used before methods of preventing blood coagulation had been found

Carrel is also renowned for his work on tissue culture With his associates, he made significant contributions to its development, and first demonstrated his tissue fragments in 1910 He was also celebrated for his methods, during the First World War, of treating deep wounds by constant irrigation with a mild antiseptic and for the development of a mechanical heart which was announced in 1935 Many advances in biology and medicine grew out of his work.

## 1913

### RICHET, CHARLES ROBERT

Nationality French

b August 26, 1850, Paris, d December 4 1935, Paris

*In recognition of his work on anaphylaxis*

Richet, the many faceted doctor, was educated in Paris and was the Professor at the faculty of Medicine at Paris A distinguished man of letters, he won great literary reputation as a writer on scientific subjects and international peace under the pen name of Charles Epheyre

He was awarded the Nobel Prize for his works on anaphylaxis , a term he used to describe a phenomenon noted earlier by Theobald Smith i e , a hypersensitive reaction (similar to allergy) to injections of foreign proteins His work on the physiology of respiration and digestion is

significant Richet discovered that hydrochloric acid is the main component of gastric juice He worked also on serum therapy, animal heat and the nervous system

1914

BARANY, ROBERT

Nationality Hungarian

b April 22, 1876 Vienna, d. [illegible] 8, 1936, Uppsala Sweden

*For his work on the physiology and pathology of the vestibular apparatus*

Barany joined the department of Otology in Vienna after obtaining his M D from the same University He was taken a prisoner by the Russians in 1915, while serving as a doctor in World War I, and was released in 1916 through the intervention of the Swedish Red Cross

Barany did extensive investigations on the physiology and pathology of the inner ear and cerebellum He developed a method for accurate diagnosis of one-sided deafness He headed the ear, nose and throat clinic of his University, Uppsala, for about two decades until his death

## 1915, 1916, 1917 and 1918

Not awarded

## 1919

BORDET, JULES

Nationality Belgian

b June 13 1870, Soignies Belgium d April 6, 1961, Brussels

*For his discoveries relating to immunity*

Bordet's work on blood corpuscles and the destruction of bacteria in the blood serum constituted the founding of Serology Bordet graduated in Medicine in Brussels in 1892 and taught there from 1901 At the Pasteur Institute in Paris, he found that when blood serum is heated to 55 C, it loses its ability to destroy bacteria, but its antibodies are not destroyed He rightly deduced that some heat-sensitive component of serum, which Ehrlich called complement , is necessary Bordet demonstrated subsequently, in 1901, that this is used up when an antibody reacts with an antigen, a process called "complement fixation' and of importance to immunology It is now known that the immune system contains nine varieties of complement each an enzyme system which is responsible for the destruction of a range of pathogens

1920

KROGH, SCHACK AUGUST STEENBERGEN

Nationality Danish

b November 15, 1874, Grenna, Denmark, d September 13 1949, Copenhagen

*For his discovery of the capillary motor regulating mechanism*

It is in the realm of human physiology — the physiology of respiration and the distribution of blood to the tissues — that Krogh's work is very important. In 1904 Christian Bohr (1855-1911) had shown that the oxygen dissociation curve of haemoglobin differs in its shape from that of blood. In the same year, with K. A. Hasselbalch and Krogh, he made the important discovery that the dissociation curve of haemoglobin is greatly influenced by the partial pressure of carbon dioxide present. As the blood takes up carbon dioxide in the capillaries, there is an increased liberation of oxygen from oxyhaemoglobin.

About 1908 Krogh developed his micro-aerotonometer, so that the gaseous exchange between a single bubble of air and blood flowing round it could be easily determined. Using his aerotonometer Krogh, with his wife, showed that the arterial oxygen pressures were always below the oxygen pressures in the alveolar air and he concluded that gaseous exchange in the lungs is always due to diffusion. Part of the argument for secretion had been based on the sequence of events in the swim-bladders of fishes. In 1911 Krogh working on lower marine forms which also maintained their relative positions despite changes in water pressure, showed that there is no secretion of oxygen into their air sacs.

In man, Krogh calculated the quantity of oxygen which should theoretically diffuse across the walls of the pulmonary alveoli and he showed that this amount was equal

to the exchange of gas actually found, and that this correspondence applied even when there was an extreme demand for oxygen These results were effectively the death blow to the secretion theory In 1912 Krogh, in collaboration with Johannes Lindhard (1870-1947), worked out the nitrous oxide method of measuring the circulation rate in man

Krogh next turned his attention to the capillaries By ingenious calculations he showed that the oxygen tension in muscle is only slightly below that in the capillaries, even when the muscle is intensely active He then confirmed his theories by experiments on the frog's tongue and in other ways He found that when a muscle is at rest the number of capillaries seen on examination is relatively small But as soon as the muscle is stimulated many hitherto unseen capillaries open up become filled with blood, and then disappear on the cessation of activity He showed that such effects are not due to increased pressure in the vessel supplying the capillary field on the contrary, the capillaries are in a constant state of tonus, which keeps them constricted But as soon as there is a demand for more blood to a part, such as on the stimulation of a muscle the tonus is relaxed the capillary opens up and is filled with blood

## 1921

Not awarded

1922

## HILL, ARCHIBALD VIVIAN

Nationality British

b September 26, 1886, Bristol, England, d June 3, 1977, Cambridge

*For his discovery relating to the production of heat in the muscle*

Hill was a physiologist engaged in biophysical studies and did pioneering work on energy exchanges during nerve and muscular activity After a brief period of theoretical and experimental work on drug and enzyme kinetics, Hill began to develop methods for the study of mechanical and thermal energy exchanges during muscular contraction and their relation to the chemical process in muscle tissue This work was interrupted by the First World War, during which Hill served in the Army as a Major, founding and directing an Anti aircraft Experimental Section

Hill was one of the scientific leaders of his generation He is remembered by many colleagues and pupils not only for his scientific discoveries but for bringing physiochemical ideas and high precision measurements to bear on biological problems and above all for inspiring and encouraging his young colleagues and for the lead he took during the Nazi period in helping those who had been driven from their laboratories by political or racial persecution

MEYERHOF, OTTO FRITZ

Nationality German

b April 13 1884, Hanover, Germany d October 6, 1951, Philadelphia

*For his discovery of the fixed relationship between the consumption of oxygen and the metabolism of lactic acid in the muscle*

Meyerhof received his M D in medicine from Heidelberg

in 1909, and began to specialize in psychiatry, but switched to biochemistry and studied techniques to examine the chemical changes linked with muscular action He followed up the work of Hopkins, who had demonstrated that lactic acid is formed in a working muscle and showed how this is formed, and how it is removed when the muscle rests The ratio of anaerobic decomposition to aerobic recombination is today known as the 'Meyerhof quotient' In 1938 he moved to France since he was unhappy with Nazi Germany and later escaped to the U.S

## 1923

BANTING, SIR FREDERICK GRANT

Nationality Canadian

b November 14, 1891, Alliston Ontario d February 21, 1941 Newfoundland

MACLEOD, JOHN JAMES RICHARD

Nationality Canadian

b September 6, 1876, Perthshire Scotland d March 16 1935 Aberdeen

*For the discovery of insulin*

Banting, the Canadian physiologist, studied in Toronto and was a private in the army before he completed his Medicine and was commissioned A youth of robust health, he won an MC for gallantry in action in 1918 After his practice failed to take off, he took up research at Ontario University where Macleod, the Professor of the Physiology faculty, gave him facilities and a recently qualified assistant, Best, to further his interests on studies on diabetics

Macleod studied Medicine in Aberdeen and after graduating in 1898, travelled extensively in Europe and America He held positions in physiology and biochemistry at the London Hospital, Western Reserve University, Cleveland, Ohio He joined the University of Toronto subsequently as Director Physiological Laboratory

In addition to his contribution to the understanding of diabetics he had worked in various areas like purine bases carbamates tuberculosis bacterium, electric shock and air sickness A brilliant teacher, author and an excellent research worker, it was Macleod who had suggested the name of Best as a research associate to Banting

Diabetes mellitus is a disease where excess glucose appears in the blood and urine and until Banting s work (1922), it was always fatal Although it was known that diabetics was linked to the pancreas and probably to the cells in it known as the islets of Langerhans it was Banting who developed methods to isolate the unknown hormones (insulin) and demonstrated that glucose levels in blood could be regulated with insulin

Macleod was on sabbatical leave during the time when Banting assisted by Best, worked on this problem The hormonal extracts were purified with the help of a chemist, Collip, to be injected for treatment of patients

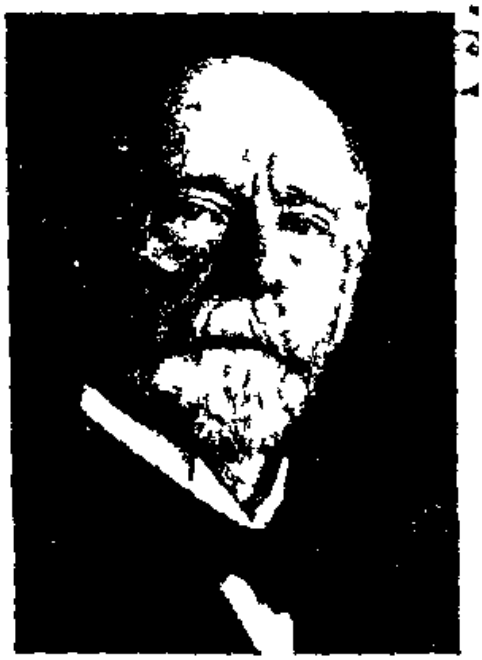
The discovery of insulin was one of the greatest moments in the annals of medical history and millions of diabetic patients have been saved with the help of insulin

The 1923 Nobel award jointly to Banting and Macleod created some controversy, since the role of Macleod in the discovery of insulin, independent of his tall status as a researcher and academic was not significant Banting was disturbed enough at the omission of Best's name that he shared half the prize amount with him Macleod, himself, shared his part of the prize amount with Collip

Banting joined the army again during World War II and was killed in an air crash He was working on war gases

Insulin was isolated in pure form in 1926 and much later, in 1966, Sanger deducted its chemical structure, it is a protein molecule, built of 51 amino acids

1924



EINTHOVEN, WILLEM

Nationality Dutch

b May 21, 1860, Semarang Java, now in Indonesia, d September 29, 1927, Leiden, Netherlands

*For his discovery of the mechanism of the electrocardiogram*

Einthoven s first papers were on the physiology of the eye on the bronchial musculature, and on the physics of the capillary electrometer Thereafter he constructed a string galvanometer and applied it to record the electrical activity of the contracting heart muscle (electrocardiography), as well as for graphic registration of the heart sounds (phonocardiography)

The electromotive changes accompanying the heart beats' had been demonstrated in 1887 by Waller, but the inertia of

the capillary electrometer did not allow more than a demonstration that there was 'a true electrical variation of the human heart' Einthoven recorded electrocardiograms not from the chest wall but from two limbs of the subject in three different combinations and these have remained the standard recordings He also described the main deflections of the tracing and devised a nomenclature

Electrocardiography is second only to the discovery of X rays by Roentgen in importance among the physical methods used in clinical medicine

## 1925

Not awarded

## 1926

FIBIGER JOHANNES ANDREAS GRIB

Nationality Danish

b April 23, 1867, Sikeborg, Denmark, d January 30, 1928, Copenhagen

*For his discovery of the spiroptera carcinoma*

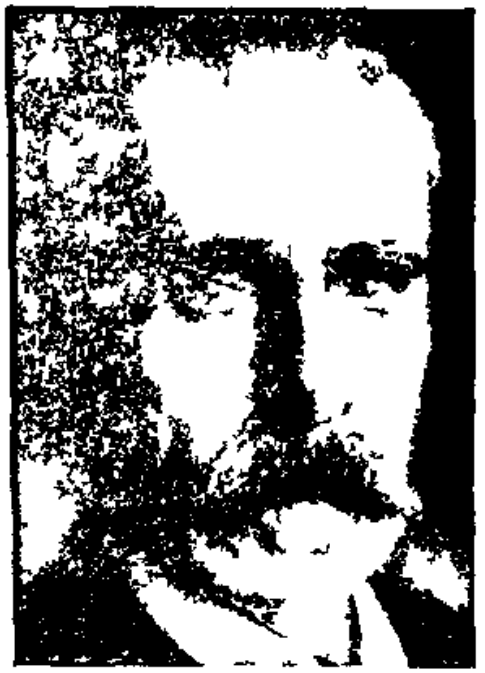
Fibiger, the Danish pathologist, studied Medicine in Berlin and later graduated from the University of Copenhagen in 1895 He afterwards became Professor of Anatomy at the Institute of Pathology

Fibiger pioneered the concept of induced cancer by producing tumors in the stomachs of rats by feeding them cockroaches infested with a certain species of West Indian nematode parasites He contributed significantly to the theory that cancer is due to constant irritation of the stomach tissue

Yamagima Katsusaburo, the Japanese pathologist followed this work by inducing cancer in laboratory animals by painting coal tar derivatives on their skin

Although the theories and interpretations of Fibiger were classic and trend setting in cancer research, his claims of cancer induction was found to be, unfortunately, false at a later date

## 1927



### WAGNER-JAUREGG, JULIUS

Nationality Austrian

b March 7, 1857, Wels, Austria d September 27, 1940, Vienna

*For his discoveries of the therapeutic value of malaria inoculation in the treatment of dementia paralytica*

Wagner Jauregg the Austrian neurologist and psychiatrist, was a pioneer of shock therapy and other treatments of mental disorders He was a Professor at the University of Vienna from 1893 to 1928 Avicenna (980-1031) had observed that certain cases of mental disorders like syphilitic insanity can be controlled by inducing febrile illness in the patient Wagner-Jauregg established that malarial fever, which could be easily induced and then regulated by quinine therapy could be effectively used for treatment of

syphilitic meningoencephalitis, or general paresis of the insane

Antibiotics have considerably replaced these methods now But Wagner-Jauregg's place as the first researcher to use shock therapy for treatment of mental patients is permanent

1928

NICOLLE, CHARLES JULES HENRI

Nationality French

*b September 21, 1866, Rouen France d February 28* 1936, Tunis

*For his work on typhus*

Nicolle, the French physician and microbiologist, was the Director of the Pasteur Institute in Tunis (1903-1932) and

had worked with Roux in Paris He had worked on several diseases including whooping cough, measles, trachoma and influenza

His study of the epidemic typhus fever got him the Nobel Prize

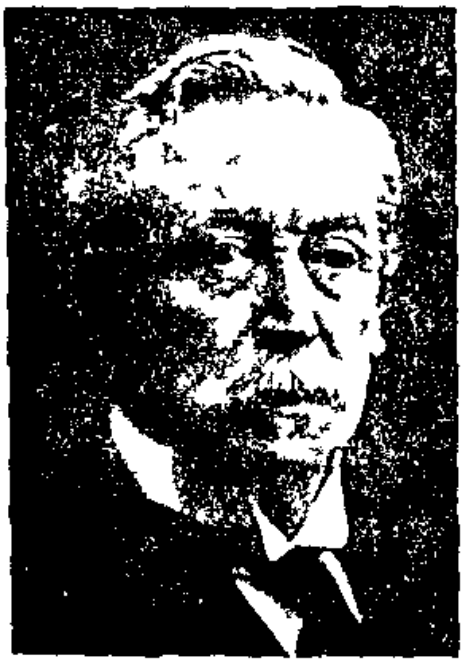
Typhus fevers are caused by the pathogens rickeltsia and the worldwide mortality rates due to this fever ranged between 10-70 percent The smaller size of these pathogens (between bacteria and viruses) helped them escape deduction until Nicolle noted that the victims infected others before they entered hospital, but stopped doing so immediately after

He deduced, rightly, that the path of infection was broken when the patient s clothing was removed and cleaned and guessed that the body louse was the vector

Further experiments with monkeys demonstrated that the louse is only infective after taking blood from a victim, and that the infection was spread through its faecal matter This classic work in 1909 resulted in massive control efforts of the lice and through that of typhus

Nicolle subsequently demonstrated that recovered patients of typhus influenza and measles had developed antibodies in them He also discovered the carrier" state, important in immunology

1929



EIJKMAN, CHRISTIAAN

Nationality Dutch

b August 11, 1858, Nijkerk Gelderlands, Holland, d November 5 1930, Utrecht

*For his discovery of the antineuritic vitamin*

A student of the Nobel laureate Robert Koch, Eijkman, started investigations on beriberi, the mortal disease that affected chicken when the infection broke out among his laboratory chicken The condition was characterized by an ascending paralysis ultimately affecting the respiratory muscles There was no evidence that the disease was due to an infection Eijkman discovered that the laboratory attendant had, for a short period, fed the birds on cooked rice obtained from the hospital kitchen Then a new cook arrived and refused to allow rice from the military hospital to

be given to the civilian laboratory This latter event coincided with the disappearance of the disease in the chicken. Eijkman then showed that the disease could be produced at will by feeding chicken on polished rice instead of on unmilled rice, and that the bran removed by polishing would cure the disease if administered with the polished rice Eijkman s work soon led to experiments by others on the feeding of prisoners in the Far East, and to the prevention and cure of human beriberi

Eijkman misinterpreted his results, he thought that the bran contained a special protein or salt or, alternatively, a protective substance against some poison Later workers in Batavia and in British India demonstrated that the bran contained an essential food factor, now known as Vitamin $B_1$ (thiamine)

HOPKINS, SIR FREDERIC GOWLAND

Nationality British

b June 20, 1861, East Sussex, d May 16, 1947, Cambridge

*For his discovery of the growth stimulating vitamins*

Hopkins's first publication (1878) was a note in an entomological journal This interest led him to a study of the pigments of butterflies' wings, which he believed to be related chemically to uric acid an intuition which was not confirmed for many years He soon distinguished himself at Cambridge by devising a method for obtaining crystalline proteins and by his classic paper (with Morley Fletcher, 1907) on the chemistry of muscle contraction A student's failure to obtain the Adamkiewicz colour reaction for proteins led Hopkins to identify glyoxylic acid as the impurity in commercial acetic acid which caused the test to succeed, and to isolate (with S W Cole, 1910) the important amino acid tryptophan from protein hydrolysates, as the fragment reacting with glyoxylic acid

Already, by 1906, studies of the relationship between growth and diet had brought Hopkins to the concept of accessory food factors (now called vitamins) He based his ideas on experiments in which addition of small quantities of milk to 'synthetic" diets restored normal growth in rats Attempts to isolate these substances were both laborious and fruitless, and were followed by a nervous breakdown in 1910, caused by disappointment and overwork.

For his part in the development of the concept of vitamins, Hopkins shared the Nobel Prize with Eijkman His greatest contribution to biochemistry was his insistence that biological problems could be solved in chemical terms, as against the ideas in vogue at that time

## 1930

### LANDSTEINER, KARL

Nationality Austrian

b June 14, 1868, Vienna, d June 26, 1943, New York

*For his discovery of human blood groups*

Karl Landsteiner began work on his life long interest, the mystery of blood at an early age after graduating from medical school and training as a chemist for four years Blood transfusions until then had been so disastrous that France Italy and England had passed laws prohibiting such experiments Landsteiner collected blood samples, allowed them to clot then separated clot from the serum On mixing the red cells of one individual to those of another, he could observe these cells agglutinating — clumping together like a bunch of grapes His momentous conclusion that all blood cells were not alike and that they can be

categorized into A, B and nought — O — revolutionized medical research later (Landsteiner missed the AB group sine none of his volunteers had this rare group in them, but two of his colleagues identified it) The pioneering work was long in waiting before being recognized as a milestone in medical sciences Singlehandedly, he had founded the field of immunochemistry

Landsteiner was such a giant of science that, in the range of his achievements he has few equals He laid the groundwork for today's polio protective vaccines He delineated the mechanism of skin allergies His work on *Rickettsia* opened the way for vaccines to prevent typhus and Rocky Mountain spotted fever

1931

WARBURG, OTTO HEINRICH

Nationality German

b October 8, 1883, Freiburg-in-Breisgau, d August 1, 1970, West Berlin

*For his discovery of the nature and mode of action of the respiratory enzyme*

Warburg, the German biochemist, was a student of Emil Ficher, and graduated in Medicine from Heidelberg in 1911 An enormously influential biochemist, he had such great names as Meyerhof and Krebs as his students He headed the Max Planck Institute of Cell Physiology until he retired at the age of 86 During World War I, he served in the Prussian Horse Guards

Warburg's major work was on intracellular respiration and he devised the Warburg manometer (or respirometer) in 1923 In this device very thin tissue slices are incubated with a buffered nutrient and their uptake of oxygen is measured by the fall in pressure He used this to study both normal cellular respiration and model systems as also the action of enzyme poisons (such as cyanide) and catalytic metals such as iron, and the activity of cancerous cells The contribution of Warburg and his students to the understanding of enzyme action, co-enzymes and the func tion of nicotinamide adenine dinucleotide (NAD), can cerous cells and photosynthesis is enormous and invaluable

A bachelor till death, Warburg tended, towards the end, to be too individualistic and intolerant of others' ideas and eventually became isolated

## 1932

ADRIAN, LORD EDGAR DOUGLAS

Nationality British

b November 30, 1889, London d August 4, 1977, London.

SHERRINGTON, SIR CHARLES SCOT

Nationality British

b November 27, 1857, London d March 4, 1952, Eastbourne, England

*For their discoveries regarding the functions of neurons*

Adrian, the English physiologist, took his M D at Trinity College (1915), Cambridge and was associated with the institution for nearly 10 years He did much to advance neurophysiology His major work was the use of thermionic valve amplifiers to reliably record nerve impulses in a single nerve fibre, and to show that they do not change with the nature or strength of the stimulus

He further demonstrated that a nerve transmits information to the brain on the intensity of a stimulus by frequency modulation, i e , as the intensity rises, the number of discharges per second in the nerve also rises Working on electrical activity of the brain, his contribution to the study of "Berger Rhythm" (after Hans Berger, 1924) opened up new areas of research in epilepsy and the location of cerebral tumors He himself (1934) studied these brainwave rhythms which result from the discharge of thousands of neurons and which can be displayed as an electroencephalogram (EEG)

An extremely active and popular figure at Trinity College, he was an excellent fencer, sailor and rock climber His works include *The Basis of Sensation* (1928), *Mechanism of Nervous Action* (1932) and *Determining Human Behaviour* (1937) He was awarded a barony in 1955

Sherrington, the English neurophysicist, studied Medicine in Cambridge, as also in Germany under Koch He was a Professor of Physiology at the University of Liverpool and London His major work was on reflex motor activity in vertebrates and he demonstrated the effect of reflex actions in facilitating the nervous system to function as a unit His work expanded the field of brain surgery As a physician he did work on cholera and diphtheria His contributions to a whole range of concepts and terminologies in neurology earned him the nickname of the William Harvey of the nervous system' The terms synapse, proprioceptor motor unit, neuron pool, etc were coined by him.

Sherrington turned to philosophic writings and poetry after retirement and his work, *Man on his Nature* (1940), is a classic His book, *The Integrative Action of the Nervous*

*Systems* (1906), became a standard reference source book.

## 1933

### MORGAN, THOMAS HUNT

Nationality American

b September 25, 1866, Lexington, Virginia, d December 4, 1945, Corona del Mar, California

*For his discoveries concerning the role played by the chromosome in heredity*

Morgan s first studies were in embryology, it was he who showed by a very simple experiment with frogs' eggs that the Roux Weismann theory of differentiation was untrue A visit to H de Vries in Amsterdam, where mutant forms of the evening primrose were growing, drew him to the subject of variation

In 1908 he started breeding mice himself, followed by rats and the fruit fly *Drosophila* At first he tried the effect of various mutagens on *Drosophila*, but without apparent success *His hybridization of these flies*, however, instead of invalidating Mendel's laws, confirmed them At the same time he found deviations from the law of independent assortment of characters Thus his first mutant ("white eye") was almost completely confined to male flies, which led him to conclude that it is the male which is heterogametic (i e, male = XY, female = XX) His second mutant ( rudimentary", i e, rudimentary wings) was also confined to the males But when he bred a race of the double mutant he obtained in their offspring all assortments of characters, as Mendel s law states, but not quite in the proportions expected if there were completely independent hereditary transmission of wing and eye characters

The initial limitation of these mutants to one sex he interpreted as due to their being determined by genes on the same chromosome The recombination between them suggested to him that chromosomes had exchanged segments in the manner suggested by Janssens in 1909 The departure from Mendelian expectation was not sufficient in this case to clinch the matter

In 1911, he discovered a considerable departure — very low percentage of recombination — between 'white eye' and 'yellow body" In a short communication to *Science* that year he put forward the chromosome theory of inheritance, *according to which* the extent of recombination obtained between genes on the same chromosome is a measure of their spatial separation Sturtevant was still an undergraduate in 1911 when, in conversation with Morgan he realized that variations in the strength of linkage

between characters gave an index to their linear sequence on the chromosome The same night he drew up the first chromosome map, which showed five sex-linked genes

Morgan and his co workers, Sturtevant, Bridges, and Muller, developed this simple theory with astonishing success, with the result that they were able to interpret the whole range of Mendelian phenomena in terms of it Morgan was a very active research worker and prolific writer In his latter years he returned to his embryological studies

1934

MINOT, GEORGE RICHARDS

Nationality American

b December 2, 1885, Boston, d February 25, 1950, Brooklyn

MURPHY, WILLIAM PARRY

Nationality American

b February 6 1892 Stoughton Wisconsin, d 1987

WHIPPLE, GEORGE HOYT

Nationality American

b August 28, 1878, As land, New Hampshire February 2, 1976, Ne York.

*For their discoveries concerning liver therapy in cases of anaemia*

The American physiologist Minot and his fellow Americ Murphy reported the results of their successful treatme of pernicious anaemia in 1926 Minot's earlier work blood disorders was continued at the Peter Bent Brigha Hospital, Boston, where he worked on the lethal diseas pernicious anaemia He retired as the Director of t Thorndike Memorial Laboratory in Boston

Following on the work of Whipple, who had demonstrated the control of excessive bleeding in dogs due to anaemia, Minot and Murphy injected raw liver into patients and effectively reversed anaemia They developed an effective liver extract for oral consumption by patients and in 1948 isolated vitamin $B_{12}$ (cyanocobolamine), a therapeutic anti-anaemic factor, from liver extract Subsequent research has revealed that pernicious anaemic patients lack a particular substance that helps absorb $B_{12}$, in their gastric juice

Murphy took his M D from Harvard University (1920) and was associated with Peter Bent Brigham Hospital in Boston from 1922. He made special studies on diabetics and diseases of the blood, particularly with reference to liver treatment for pernicious anaemia

Following graduation (1905) Whipple trained in Pathology for two years He first described a rare condition characterized by the deposition of fat in the intestinal and mesenteric lymphatic tissues subsequently known as Whipple's Disease After a year in the Canal Zone studying many tropical disease such as amoebic dysentery, filariasis, and blackwater fever, he returned to Johns Hopkins where, from 1908 to 1914, his researches centred on the liver, jaundice, and abnormal blood coagulation

In 1914 Whipple became Director of the Hooper Foundation for Medical Research and Professor of Research Medicine at the University of California in San Francisco Despite the difficulties of fitting out a new laboratory in a war-time atmosphere, he continued his studies on bile formation in dogs, gradually extending this to include haemoglobin production and, consequently, experimental anaemia, on which he published over 200 papers

He developed, with Frieda Robbins, an experimental model whereby fixed quantities of blood were removed from dogs, and the influence of various diets in the regeneration of blood cells was studied They found that liver, kidney, and meat were (in that order) particularly effective in stimulating the bone marrow to produce new red blood cells

Liver extract had already been suggested by Hooper in 1918 as particularly effective in the treatment of pernicious anaemia in human beings Hooper's findings were neglected, but following Whipple's reports, two Harvard physicians, George Minot and William Murphy, began in 1926 to systematically investigate the use of liver and other foodstuffs in the treatment of pernicious anaemia

For these researches, Whipple, Minot and Murphy shared the Nobel Prize for Physiology or Medicine in 1934 The relationship between pernicious anaemia and vitamin in B12 deficiency was subsequently elucidated by other workers

The bile pigments were always of interest to Whipple, but he also made important contributions to our knowledge of the blood proteins to the mechanism of blood clot formation and to the pathology of a genetic disorder which leads to anaemia and other sequelae Found in people of Mediterranean extraction it was first named thalassemia by Whipple in his classic (1932) description of its pathology

## 1935

SPEMANN, HANS

Nationality German

b June 27, 1869, Stuttgart, Baden Wuerttenberg d September 12, 1941, Freiburg-in-Breisgau, Germany

*For his discovery of organizer effect in embryonic development*

Spemann began his experiments with eggs of newts since the eggs of these small lizard-like animals closely followed that of the other vertebrates, including man, in their developments The basic problem that he was trying to tackle was about how cells and tissues differentiate during growth

He demonstrated that, by grafting tissues from one area of the developing embryo to another the transplanted section can transfer its organising power to its host's embryo

Spemann named this "inducing" bit of tissue "the organizer" This discovery led to the conclusion that the specialisation of the cells could be explained as an action of a special group of cells

The brilliant work and deduction of Spemann is especially significant since he did not know when he was operating so delicately on newts and salamanders that each cell carries a complete master plan for the whole individual and for all the specialised proteins needed to produce a newt, a salamander, or a human

## 1936

DALE, SIR HENRY HALLETT

Nationality British

b June 9 1875 London d July 23 1968 Cambridge

LOEWI, OTTO

b June 3, 1873, Frankfurt am Main d December 25, 1961, New York City

*For their discoveries relating to chemical transmission of nerve impulses*

Dale, the English physiologist and pharmacologist, was educated in Medicine at Cambridge, London and Frankfurt and joined the Wellcome Laboratories in 1904 Along with G Barger, he studied the physiological action of ergot (a potent extract from a fungal infection of rye) and their work led to two research areas which are linked with their names These are *histamine* a compound released by injured cells or in reaction to foreign protein, and *acetylcholine* the neurotransmitter

Dale's work on acetylcholine as agent in the chemical transmission of nerve impulses won him the Nobel Prize His work also led to the fuller understanding of allergy and anaphylectic shock. Dale was the Director of the National Institute of Medicine (1928-42) and was a major spokesman for science in the U K His writings include *Adventures in Physiology* (1953) and *Autumn Gleanings* (1954) He was knighted in 1932.

Loewi, the American physiologist and pharmacologist, was a professor of pharmacology at the University of Graz, Austria He graduated in Medicine from the University of Strassburg He was in exile during the German occupation and migrated to America in 1940, where be became Professor of Pharmacology at the College of Medicine, New York

Loewi is known for his discovery of chemical transmission of nerve impulses Working on frogs, he demonstrated the presence of an invisible reactive substance, subsequently named *acetylcholine* that could transmit nerve impulses

Loewi also worked on the metabolism of heart, kidneys and nerve system "Loewi's test" was devised by him for detection of acute haemorrhagic pancreatitis His discovery of a chemical means of conduction of nerve impulses, however, is his greatest contribution to science

## 1937

### SZENT-GYORGI VON NAGYRAPOLT, ALBERT

Nationality Hungarian

b September 16 1893, Budapest d October 10, 1986, Massachusetts

*For his discoveries in connection with the biological combustion processes with special reference to Vitamin C and the catalysis of fumaric acid*

Szent-Gyorgi graduated in Medicine from Budapest

University (1917) and completed his Ph D from Cambridge (1927), under Hopkins, on vitamins

On his return to Hungary (1930), he demonstrated that vitamin C (the anti-scorbutic vitamin, ascorbic acid) was in fact the same compound he had isolated earlier in Cambridge in 1928 His studies on biological oxidations and discovery of ascorbic acid in adrenal glands got him the Nobel Prize He identified the Hungarian papriku as a rich source of ascorbic acid

By 1935 he was working on the biochemistry of muscle and his work was later developed by Krebs on the metabolism of muscles Gyorgi also isolated two proteins from muscles (myesin and actin), which combine to form actomysin Addition of ATP (adenosine triphosphate) contracts actomysin and Gyorgi described the sight of the contraction of these artificial fibres as ' the most exciting moment of my scientific career'

Gyorgi s discoveries, leading to new understanding of the physiology of the heart are significant He was offered the presidency of Hungary in 1947, but declined the offer and migrated to the U.S

His works include, *Chemistry of Muscular Contraction* (1947), *Bioenergetics* (1957) and *Introduction to Submolecular Biology* (1960)

1938

## HEYMANS, CORNEILLE JEAN FRANCOIS

Nationality: Belgian

b March 28, 1892 Ghent, Belgium d July 18, 1968 Knokke

*For the discovery of the role played by the sinus and aortic mechanisms in the regulation of respiration*

Belgian physiologist Heymans was educated at the University of Ghent and studied physiology further in Europe and U.S.A. In 1925, he succeeded his father, J.F. Heymans, as Professor of Pharmacology at Ghent.

His investigations into the circulatory and respiratory systems led him to the discovery of 'pressor receptors', a set of sensory organs in the wall of the Carotic Sinus which is an enlarged portion of the carotid artery near its bifurca

tion He also discovered a set of "chemoreceptors or 'glomera' at the base of the aorta, near the pressor receptors Glomera monitor the oxygen content of the blood They also help in regulating breathing through the respiratory centre at the base of the brain

## 1939

DOMAGK, GERHARD

Nationality German

b October 30, 1895, Lagow, Brandenburg, d April 24, 1964, Elberfeld, Germany

*For the discovery of the anti-bacterial effects of prontosil*

Domagk embarked upon a systematic search for chemical agents capable of destroying bacteria within the human body In 1932 he made the outstanding discovery that

Prontosil Red, a dye containing a sulphonamide group, could control streptococcal infections in mice

This result was not, however, published until 1935, possibly because of difficulty in repeating the results Subsequently, it was found elsewhere that the antibacterial activity was specifically associated with the sulphonamide grouping and not with the dye stuff itself

This discovery opened the way to the cheap and effective treatment of a variety of highly pathogenic infections Dramatically, one of those whose life was saved was Domagk s own daughter, who accidentally infected herself in the laboratory

The Nazis forbade him to accept the Nobel Prize in 1939, eventually (1947) he received the medal but not the Prize

## 1940, 1941 and 1942

Not awarded

## 1943

### DAM, HENRIK CARL PETER

Nationality Danish

b February 21, 1895, Copenhagen, d April 1975, Copenhagen.

*For his discovery of vitamin K*

Dam graduated from the Polytechnic Institute of Copenhagen (1920) and took his Ph D in Biochemistry from the University of Copenhagen (1934) After working with Nobel laureates Pregl and Karrer, he went to America in 1940 and was mainly at the University of Rochester, New York until he returned to Copenhagen as Professor of Biochemistry at the Polytechnic Institute

Dam s major contribution was his discovery of vitamin K (koagulations-vitamin) Working with alfalfa hay, he and

Doisy, independent of each other, reported the isolation of this vitamin Dam was working on a deficiency disease in chicks which led to excessive bleeding, delayed coagulation and thus decreased blood clotting He demonstrated that this was due to the lack of a fat-soluble anti haemorrhagic vitamin, which he isolated and named vitamin K

DOISY, EDWARD ADELBERT

Nationality American

b November 13, 1893, Hume, Illinois d October 23, 1986, St Louis

*For his discovery of the chemical nature of vitamin K*

The American biochemist Doisy, was educated in Illinois and took his Ph D from Harvard University in 1920 He worked with the embryologist, Edgar Allen, and spent most of his life at St Louis University Medical School, Missouri

Doisy's earlier works were on sex hormones and in 1923 he devised a bioassay for the female sex hormone and secured potent extracts Butenandt isolated the first oestrone Doisy's major work was based on the study of vitamin K the deficiency of which results in failing blood coagulation He isolated the K factor (K for Koagulation) from alfalfa grass and a related but different K factor from putrefied fish meal He also demonstrated these two anti-haemorrhagic vitamins $K_1$ and $K_2$ as derivatives of 1,4-napthoginnone Vitamin $K_1$ and $K_2$ are valuable in therapy, for example, in reducing bleeding in a patient with an obstructed bile duct

Doisy's books include *Sex and Internal Secretions* (1930) and *Sex Hormones* (1936) His contribution to the knowledge of vitamins antibiotics hormones and blood buffers is enormous and in 1955 the University honoured him by naming his department after him

1944

ERLANGER, JOSEPH

Nationality American

b January 5, 1874 San Francisco, d December 5, 1965, St Louis, Missouri

GASSER, HERBERT SPENCER

Nationality American

b July 5, 1888, Platteville, Wisconsin, d May 11, 1963, New York City

*For their discoveries relating to the highly differentiated functions of single nerve fibres*

Erlanger graduated in Chemistry from the University of California and took his M D from Johns Hopkins University in 1899 He was Professor of Physiology at Washington University when he began his collaborative work with his student Gasser on the application of modern electronics in the study of the electrophysiology of nerves They used a low voltage cathode ray oscillograph and observed the characteristic wave pattern of the nerve impulses of the

nerve fibres on the screen Different nerve fibres have different conductivity ratios, depending on the thickness of the fibre Each nerve fibre also requires a stimulus of varying intensity (threshold) to create an impulse Different fibres transmit different kinds of impulses, represented by different types of waves in the oscillograph

Gasser graduated from the University of Wisconsin in 1910 and obtained his M D from Johns Hopkins Medical School in 1915 He worked with Erlanger earlier and rejoined him at Washington University, where he became a Professor of Pharmocology in 1921 Neurophysiology, the world over, has tremendously benefitted from these studies Researches on reflex action and the mechanism of pain have advanced considerably due to their contributions

1945

CHAIN, SIR ERNST BORIS

Nationality· British

b June 19, 1906, Berlin, d August 12, 1979, Ireland

FLEMING,
SIR ALEXANDER

Nationality British

b August 6, 1881 Lochfild near Darvel, Ayrshire, Scotland, d March 11 1955 London

FLOREY, HOWARD WALTER

Nationality British

b September 24, 1898, Adelaide Australia, d February 21, 1968 Oxford

*For the discovery of penicillin and its curative effect in various infectious disease*

The German British biochemist Chain, studied physiology and chemistry in his native Berlin and worked under Hopkins in Cambridge University He moved subsequently to

Oxford, where he joined Florey's staff working on penicil lin Their work, along with that of N G Heatley, on the production, isolation and testing of the mould product penicillin proved tht it is a valuable antibacterial In 1948 he moved to Rome and in 1961 to the Imperial College, London.

Florey's work on penicillin led him to discover the enzyme that destroys it (penicillinase) He later worked on developing strains of penicillin resistant to penicillinase

Fleming was associated with two major discoveries — lysozyme and penicillin

The discovery of lysozyme was made in 1922, when he showed that the nasal secretion has the power of dissolving (or lysing) certain kinds of bacteria Subsequently, he showed that the active enzyme lysozyme, was present in many tissues of the body but, unfortunately, its activity was limited so far as the pathogenic organisms that cause disease are concerned

Nevertheless, lysozyme did strikingly demonstrate the possibility of the existence of susbstances harmless to the cells of the body but lethal to bacteria — the magic bullets' sought with only limited success from the time of Paul Ehrlich

Fleming noticed in 1928 that a culture of staphylococcus had become accidentally infected with a mould, subsequently identified as *Penicillium notatum* Around the mould colony, the staphylococci had disappeared, and Fleming correctly attributed this to the production of an anti bacterial substance by the mould

Carefully, he isolated the mould and grew it in pure culture in broth, he found that after a few days the broth had acquired a high antibacterial activity He tested the sensitivity to the broth of a wide range of pathogenic bacteria, and noted that many of them were quickly destroyed by it

He also showed that white blood corpuscles were little, if at all, sensitive to penicillin broth this was a fair indication that body cells generally would not be affected by it He put the broth to practical use in separating pure stains of bacteria, and in treating local infections

In his early work, Florey made important contributions to knowledge of the lymphatic system and of Brunner's glands in the duodenum Later, he returned to research on the vascular system and explored the changes invovled in atherosclerosis

After 1958 he made extensive use of the electron microscope to study the way in which susbtances pass through the endothelial barrier between the intravascular and extravascular spaces His views and achievements gave a new outlook to experimental pathology

Florey was a man without vanity He went out of his way to present the discovery of the chemotherapeutic properties of penicillin in its right perspective and to give credit to all those who had played essential parts in the work

1946

## MULLER, HERMAN JOSEPH

Nationality American

b December 2 1890, New York City d April 5, 1967
Bloomington, Indiana

*For the discovery of the production of mutations by means of X-ray irradiation*

Muller was one of the greatest biologists of this century Remembered primarily for his work demonstrating that ionizing radiation caused mutation Muller had numerous other scientific accomplishments of great significance to his credit

He was the first to locate a gene on the fourth and last romosome of *Drosophila* He had the first demonstration, 1916 of a balanced lethal system He demonstrated

multiple crossing over in fruit flies And he demonstrated that much of the evolutionary change in organisms was due to modifier genes Throughout his research career, the role of mutation in gene expression and the nature of the gene itself were the major foci of his research

In his work with radiation, Muller came to realize that we were increasing our rate of mutations by nuclear weapons testing and medical and industrial applications of radiation technology Muller knew tht the overwhelming majority of mutations were deleterious to living things

He forcefully, and shockingly, used to point this out in his evolution course which he taught at Indiana University Prior to class, he would purchase a very inexpensive pocket watch During his lecture he would point out that mutation is change and most changes to a well adapted organism like a change to a fine piece of machinery, would be deleterious With that, he would take out his pocket watch and smash it down on the table top, demonstrating what a 'random change would do to a fine piece of machinery or, by analogy, what a mutation might do to an organism No biology education at Indiana was complete without Professor Muller's course

## 1947

CORI, CARL FERDINAND

Nationality American

b December 5, 1896, Prague Czechoslovakia, d 1984

CORI, GERTY THERESA

Nationality American

b August 15, 1896, Prague d October 26, 1957, St Louis, Missouri U S A

*For their discovery of the course of the catalytic conversion of glycogen*

Ferdinand Cori was born in Czechoslovakia and graduated in Medicine from Prague in 1920 He married his classmate, Gerty Radnitz, the same year They moved to the U S in 1922 and formed a team until Gerty's death in 1957

At Washington University, where the Corns had taken appointment in 1931, they did their best known joint research on the conversion of glucose to glycogen in the animal body and the reverse breakdown

Clem de Bernad, the French physiologist, had, as early as 1850, shown that glycogen forms an energy reserve held in the liver and muscles, which is converted to the simple sugar, glucose, when the body needs further energy

The Corns discovered the precise steps involved in this essential biochemical process, and revealed the role of the sugar phosphates for the first time The details of this process were further worked out by Fnty Lipmann

Corn was Professor of Pharmacology and of Biochemistry at Washington University Medical School until his retirement in 1966

Gerty Radnitz Corn graduated from the Medical School of Prague University in 1920, and moved with her husband to America in 1922, where she took up an assignment at New York State University In 1931 she, along with her husband Corn, moved to Washington University, where she became a Professor of Biochemistry in 1947

injections of the pituitary extract induces symptoms of diabetes Working on dogs in which diabetics had been induced by excision of the pancreas, he showed that removal of adenobyophysis made the animal extremely sensitive to insulin, thereby relieving the symptoms of the disease

Houssay was the Founder-Director of the Institute of Biology and Experimental Medicine, Buenos Aires An activist against the dictatorial junta regime of General Juan Peron, he was dismissed form service and had to survive on his medical practice The state endowment for the Nobel award was also denied to him, but he refused promising opportunities abroad and stayed on in his motherland

1948

MULLER, PAUL HERMANN

Nationality Swiss

b January 12, 1899, Olten, Switzerland, d October 12, 1965, Basel

*For his discovery of the high efficiency of DDT as a contact poison against several arthropods*

Muller, the Swiss chemist, was educated in Basle He spent his career from 1925 with the Swiss chemical company of J R. Geigy

His search from 1935, for a cheap and easily producible insecticide which would also be rapid persistent and harmless to plants and warm blooded animals, ended in his patenting an insecticide, dichloro diphenyl trichloro methane, or the commonly known DDT, in 1940 DDT was first synthesized by the German chemist Zeidler in 1873

DDT was successfully field tested against the Colorado potato beetle by the Swiss government and the U S Agricultural Department It was also highly effective in eliminating the lice carriers of typhus fever and thereby preventing epidemics at the end of World War II

The insecticide resistance developed by insects, as also the damage caused to the ecology by DDT, however resulted in adverse criticism of the product after two decades By 1970, many advanced countries banned the use of DDT

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1949

HESS, WALTER RUDOLF

Nationality Swiss

b March 17, 1881, Frauenfeld, Switzerland, d August 12, 1973, Locarno

*For his discovery of the functional organisation of the interbrain as a coordinator of the activities of the internal organs*

The Swiss neurophysiologist, Hess, studied Medicine in five Universities in Switzerland and Germany before becoming an ophthalmologist However, he switched to the subject of Physiology at the University of Bonn and headed the department at the University of Zurich from 1917-51

He pursued his interests in the autonomous nervous system with the help of precision surgery he had picked up as an ophthalmologist The autonomous nervous system

controls involuntary functions such as breathing, blood pressure, temperature and digestion

A fine insulated wire with a bare end was inserted in cats, which were under anaesthetic, in such a way that the bare end was at a defined point in the midbrain As the animal regained consciousness, he could, by passing a small current, induce different reactions such as sleep, rage, evacuation and changes in blood pressure and respiration in the animal He located the seat of autonomic function at the base of the brain, in the medulla oblongata and the diencephalon, and particularly at the hypothalamus The work led to the detailed mapping of the brain and the relating of physiology to psychiatry

**MONIZ, ANTONIO CAETANO DE ABREV FREIRE EGAS**

Nationality Portuguese

b November 29, 1874, Avanca, Portugal, d December 13, 1955, Lisbon

*For his discovery of the therapeutic value of leucotomy in certain psychoses*

Moniz was the professor of neurology at the University of Lisbon and is considered to be the founder of psychosurgery His work on the development of cerebral angiography in the late 1920s revolutionaized the diagnostic aspects of intracranial diseases

In 1936, Moniz along with Almeida Lima performed the first "prefrontal lobotomy' operation This reasoned that severance of nerve fibres between the apex of the frontal lobes, known to be associated with psychological responses, and the thalamus in cases like schizophrenia and paranoia, would cause a transformation into normal mental activity The side effects of lobotomy also made him cautious that it be done only in extreme cases where every other treatment had failed

Moniz, who was politically active was a Protuguese Minister several times

## 1950

### HENCH, PHILIP SHOWALTER

Nationality American

b February 28, 1896, Pittsburg, Pennsylvania d March 30 1965 Ocho Rios, Jamaica

### KENDALL, EDWARD CALVIN

Nationality American

b March 8, 1886, South Norwalk Connecticut d May 4, 1972 Princeton New Jersey

REICHSTEIN, TADEUS

Nationality Swiss

b July 20 1897, Wloclawek, Poland

*For their discoveries relating to the hormones of the adrenal cor tex their structure and biological effects*

Hench graduated in Medicine from the University of Pittsburg in 1920 and joined the faculty of Mayo Clinic in Minnesota Working on arthritis, he noticed that patients with jaundice or pregnant women suffered less from arthri tal pains His investigations, along with Kendall, led to the use of cortisone and adrenocorticotropic hormone (ACTH)

Kendall studied Chemisty at Columbia University, New York and thereafter worked mainly at the Mayo Founda tion in Rochester, Minnesota Thyroxin, a new amino acid,

was isolated by him from the thyroid gland Thyroxin contains iodine, and it is a component of the thyroid hormone (thyroglobulin) that plays a regulating role in body metabolism In the 1930s he isolated a series of steroids from thyroid glands and one of them, Cortisone', was shown to relieve the symptoms of rheumatoid arthritis by his coworker Hench By 1943, over 23 cortisteroids had been isolated in the U S and Switzerland and Kendall and others had devised synthetic routes to make related compounds

Reichstein was a student of Staudinger He graduated from Zurich in 1922. He collaborated with Kendall and Hench in their work on the hormones of the adrenal cortex which culminated in the isolation of cortisone as also its therapeutic application in treatment

1951

THEILER, MAX

Nationality South African

b January 30 1899, Pretoria, South Africa d August 11, 1972, New Haven, Connecticut

*For his discoveries concerning yellow fever and how to combat it*

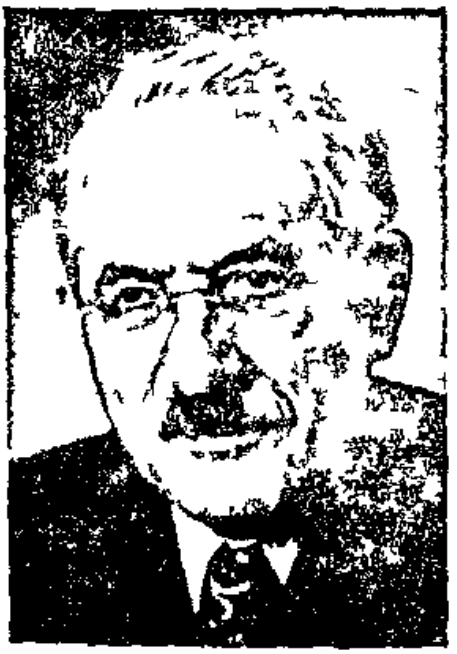
Theiler, a South African research physician was educated at the University of Capetown and in Switzerland After training at the St Thomas Hospital, London, he graduated from the London School of Hygiene and Tropical Medicine in 1922.

His research at the Harvard Medical School (1922-1930) and at the Rockefeller Institute for Medical Research, New York City (1930-1964), included encephalomyelitis and other viruses associated with tropical diseases

His work on yellow fever fetched him the Nobel Prize His discovery that mice are susceptible to yellow fever facilitated an ideal laboratory animal for the study of the disease and eventually led to the development of the vaccine against the disease His studies led to the development of the first attenuated strain of the virus

At the Rockefeller Institute, Theiler and his associates developed the improved (17-D) vaccine, widely used for human immunization against yellow fever, the deadly viral disease carried by the *Aedes* mosquito, especially *Aedes aegypti*

## 1952



### WAKSMAN, SELMAN ABRAHAM

Nationality American

b July 22 1888, Priluka, now Ukraine, d August 16, 1973, Hyannis Massachusetts

*For his discovery of streptomycin, the first antibiotic effective against tuberculosis*

Waksman, one of the foremost authorities in soil microbiology, started his life in difficulty as a young Jewish boy in Ukraine In 1910, he migrated to the U S and did his Ph D in California in Biochemistry He spent most of his career at Rutgers University, New Jersey, and was a Professor of Soil Biology

His systematic search for soil antibiotics since 1939 resulted in the isolation of the new antibiotic, streptomycin, from

the soil organism *Streptomyces griseus*, in 1943 Streptomycin destroys the human tubercle bacillus and became a major and effective drug for combating tuberculosis

Waksman isolated a number of antibiotics from soil bacteria like actinomycin, which though toxic to some animals, is used in the treatment of cancer Several other antibiotics like neomycin are also the work of Waksman and his team. The term "antibiotics' was first coined by him in 1941 His works include his autobiograph, *My life with the Microbes* (1951), and a most exhaustive and authoritative book, *Principles of Soil Microbiology* (1927)

1953

KREBS, HANS ADOLF

Nationality British

b August 25, 1900 Hildesheim, Germany, d November 22 1981, London

*ır his discovery of the citric acid cycle*

LIPMANN, FRITZ ALBERT

Nationality American

b June 12, 1899, Koenisburg Germany, d 1986

*For his discovery of co enzyme A and its importance for intermediary metabolism*

In the early years of the twentieth century the German chemist Frany Knoop had suggested that the fatty acids — the products into which the ordinary fats of foods are broken down — are 'burned' by the removal of two carbon atoms at a time in a four-step process of oxidation The Nobel laureate Otto Warburg, at about the same time had found that an iron-containing catalyst is necessary to 'activate ordinarily inert oxygen and bring it into the

combustion process A third scientist, Heinrich Wieland, also a Nobel laureate came forth with proof that the critical step in the whole combustion process is not the oxidatio but the removal of hydrogen from the foodstuffs

In the latter part of the 1920 s David Kelin of the University of Cambridge proved that all these three men were partly right In combustion hydrogen has to be removed two atoms at a time but to make this possible oxygen has to be used and it must first be activated by a catalyst The true essence of the system is the production and transfer of energy Exactly how this was accomplished remained unknown and laboratories all around the world were seeking a solution In the late 1940 s Krebs who had left Germany to become a Professor of Biochemistry at the University of Sheffield in England worked out exactly what happens — the five steps known as the citric acid cycle in which pyruvic acid the breakdown product of the sugars and starches is broken down into carbon dioxide and water, and energy is steadily released

The key intermediary in the intraconversion of these acids was citric acid Acetyl coenzyme A produced during glycolysis reacts with a four carbon compound oxaloacetic acid to yield the six carbon citric acid The citric acid is then transformed in a series of reactions to other six five and four carbon carboxylic acids Two molecules of carbon dioxide, the gaseous waste product of cell metabolism, are released in the series Hydrogen atoms are also removed from certain acid molecules and are transferred to another complex series of reactions known as the electron transport chain There they combine with molecular oxygen to produce water and more energy At the conclusion of the citric acid transformations oxaloacetic acid is regenerated

and the cycle is ready to be repeated with the introduction of another molecule of acetyl coenzyme A

The cycle sequence of reactions outlined here is now referred to as the Krebs cycle (in honor of its discoverer ), the citric acid cycle (because of the special role of that compound), or the tricarboxylic acid cycle

During the same years Lipmann, who had also left Germany and was then Professor of Biochemistry at Harvard, discovered another substance that played a critical role in the power production of the cell He named it coenzyme A, and it was isolated a few years later, in 1951, by Feoder Lynen of Germany

1954

ENDERS, JOHN FRANKLIN

Nationality American

b February 10, 1897, Connecticut, d September 8, 1965

ROBBINS, FREDERICK CHAPMAN

Nationality American

b August 25, 1916, Auburn, Alabama

WELLER, THOMAS HUCKLE

Nationality American

b June 15, 1915, Ann Arbor, Michigan

*For their discovery of the ability of poliomyelitis viruses to grow in cultures of various types of tissue*

The American virologist Enders, whose pioneering culturing of viruses revolutionized the field of virology, had a change of several careers before finally settling down to his favourite area He was, in turn, a flying instructor, an estate

agent, took a language course at Harvard for four years and, finally, made the change to microbiology at the Harvard Medical School and took a Ph D in 1930

His interest switched to the culturing of viruses which was then being done on live chick embryos By the use of penicillin to stop the multiplication of bacteria, Enders theorised that viruses could be cultured in living cells In 1948, together with Robbins and Weller, he cultured the mumps virus using a homogenate of chick embryo cells and ox serum with added penicillin This was followed by culturing of the polio virus (1949), and the measles virus (1950) The vaccine the trio developed for measles (1951) came into widespread use in 1963

Robbins graduated from the Harvard Medical School (1940) and joined Enders in 1948 His main work was on the cultivation of the poliomyelitis virus in tissue culture His work on the viruses of mumps are also well known

Weller, a student of Harvard Medical School, joined Enders in 1939 as a tutorial student and was introduced to the field of virology and tissue culture techniques After a stint in the army, he rejoined the Enders group in 1947 He isolated the viruses reponsible for *Varicella* and *herpes Zoster* and developed diagnostic tests for them He also demonstrated that a single virus caused both these diseases

## 1955

### THEORELL, AXEL HUGO TEODOR

Nationality Swedish

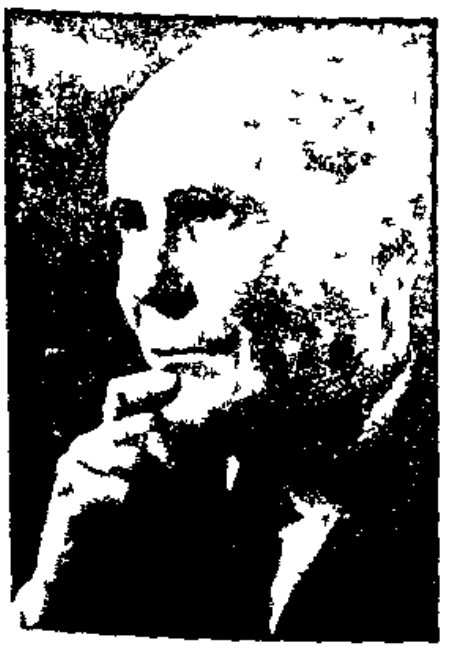
b July 6 1903 Linkoping Sweden d August 18 1982.

*For his discoveries concerning nature and mode of action of oxidation of enzymes*

Theorell did his M D in Medicine at the Caroline Institute in 1930 He joined the University of Uppsala as assistant professor in biochemistry and became Professor in 1937 His major work was on the oxidation of enzymes He was the first to isolate and purify the crystalline myoglobin, an oxygen-carrying protein found in red muscle At the Kaiser Wilhelm Institute in Berlin he worked with Nobel laureate Warburg Theorell found that an enzyme is made up of a non-protein co-enzyme and a protein apo-enzyme and that the co-enzyme facilitates oxidation of glucose by binding a

hydrogen atom at a specific site on the riboflavin molecule This proved the effect of an enzyme on the chemical activity of specific atoms and led to the study of enzymes that facilitate oxidation reactions in living cells and ways in which nutrients are utilized by organisms in the presence of oxygen to produce energy Theorell later worked on the oxidative enzyme cytochrome C and its structure His work on alcohol-dehydrogenase paved the way for sensitive blood tests that are widely applied in the legal determination of drunkenness He became the head of the Nobel Institution at Stockholm towards the end of his career

1956



COURNAND, ANDRE FREDERIC

Nationality American

b September 24, 1895, Paris, d February 19, 1988, Great Barrington Massachusetts

FORSSMANN, WERNER

Nationality German (FRG)

b August 29 1904, Berlin, d June 1 1979 Schopfheim

RICHARDS JR, DICKINSON W

Nationality American

b October 30, 1895, Orange, New Jersey, d February 23 1973, Lakeville, Connecticut

*For their discoveries concerning heart catheterization and pathological changes in the circulatory system*

Forssmann studied medicine at the University of Berlin and graduated in 1929 when he joined the August Victoria Home near Berlin His catheterization technique was developed at this hospital He worked as a urologist at Bad Kruzmack (1950-1958) and the Evangelical Hospital at Dusseldorf (1958-1961) He joined Johannes Gutenberg University Mainz as a Professor of Urology and Surgery in 1961

Forssmann was interested in the problem of reducing or avoiding the likely dangerous consequences of damaging a coronary artery or the pleura during intracardial injections The venous system is so designed that blood vessels from any point always lead to the right heart Forssmann, working on cadavers, introduced a catheter into a vein in the arm and passed it into the heart The tip of the probe without any difficulty, landed right in the heart As a next step, he decided to experiment on himself even after his colleagues refused to collaborate After applying a local anaesthetic at the elbow, he opened a vein and passed in the catheter inch by inch until its tip reached his right ventricle With the aid of a mirror, he was able to see, in the X ray, the tip of the probe in his heart This work opened up tremendous possibilities like exploring the heart with a probe in order to detect abnormalities, measuring the pressure in the different parts of the heart, and taking X-ray pictures of the heart by injecting opaque substances The recognition due to this great doctor and humanitarian came twenty five years after his discovery

Cournand graduated from the University of Paris in Medicine (1930) and moved to the Bellevue Hospital, New York City He was a Professor at Columbia

Richards began his research at the College of Physicians and Surgeons, Columbia, where he had moved after his studies in England (1928) At Columbia, where he was a Professor Emeritus (1945-1961), he started his collaborative research with Cournand on the use and perfection of cardiac catheterization', a technique to help measure the pressure and gaseous condition of the blood inside the heart, using the Forssmann method of introducing a flexible catheter into the elbow vein

Their study contributed to the understanding of the functioning of the diseased human heart as also the diag nosis of its structural defects

1957

BOVET DANIEL

Nationality Italian

b March 23 1907 Newchatel Switzerland

*For his discoveries relating to synthetic compounds that inhibit the action of certain body substances and especially their action on the vascular system and the skeletal muscles*

Bovet the Swiss-Italian pharmacologist, was educated at the University of Geneva and took his D Sc in 1929 He moved to the Pasteur Institute in Paris and became the head of the therapeutic chemistry laboratory in 1936 In Paris he was a member of the team which isolated

sulphanilamide, which is a therapeutically effective substance in the antibacterial drug prontosil Sulphanilamide was cheap, unpatented and its derivatives have been widely used against streptococcal infections Bovet s subsequent discovery of compounds which antagonize the action of histamine paved the way to widespread use of them for the relief of allergic symptoms and related conditions like the common cold He developed a surgical anaesthetic derived from curare, the South American Indian nerve poison, which is a muscle relaxant used in major surgeries

1958

BEADLE, GEORGE (WELLS)

Nationality American

b October 22 1903 Wahoo Nebraska

TATUM, EDWARD LAWRIE

Nationality American

b December 14, 1909 Boulder Colorado d November 5 1975, New York City

*For their discovery that genes act by regulating definite chemical events*

LEDERBERG, JOSHUA

Nationality American

b May 23 1925 Montclair New Jersey

*For his discoveries concerning genetic recombination and the o ganisation of the genetic material of bacteria*

George W Beadle helped found the field of biochemical genetics His most important contribution to genetics was his use of an organism in which gene function (at a biochemical level) could be studied experimentally His demonstration of the one gene one enzyme concept opened a new path of biological research by unlocking the secret of *how* genes act as controllers in biochemical path

ways At the California Institute of Technology, Beadle interested Tatum in joining the laborious work of identifying chemical disturbances underlying inherited abnormalities The idea was to select an organism, such as a fungus that has simple nutritional requirements, and induce mutations in it that observably alter these requirements By making one of the genes defective, they hoped to discover the functioning of genes

Within a few years more than eighty thousand spores of red bread mold — Neurospora — were grown in their laboratory By exposing the spores to X-rays, they demonstrated that the genes could be manipulated to change the ability to make vitamin B 6 the nutrient required to grow Further, these mutated disabilities were shown to be passed on to progenies Further experiments by them demonstrated that a change in a gene produced a direct change in the way molds and men produced materials essential to their lives a change in a gene also affected the paths that had to be undeviatingly followed in the grand process The gene determined not only how the living edifice was built, but also how it ran

Lederberg, a former associate of Tatum had in the meantime, along with Zinder, demonstrated the concept of 'transformation' by crossing two strains of a bacterium The implications were that a virus was picking up the DNA of one bacterial strain and carrying it into another bacterium In effect, the viruses that cause many human diseases can carry genetic material from one cell to another The discovery of a new genetic mechanism was a matter of great importance to genetic studies and Lederberg then only thirty three, was one of the youngest Nobelists in history

## 1959

### KORNBERG, ARTHUR

Nationality American

b March 3 1918 Brooklyn New York

*For his discovery of the mechanisms in the biological synthesis of ribonucleic acid and deoxyribonucleic acid*

### OCHOA, SEVERO

Nationality American

b September 24, 1905 Luarca Spain

*For his discoveries concerning genetic recombination and the organisation of the genetic material of bacteria*

After a brief stint with Ochoa in New York University, Kornberg moved to Washington University and both pursued their interest in the synthesising of DNA While Ochoa worked on enzymes that might play a part in the fashioning of RNA Kornberg studied those that might put together the separate building blocks or units of DNA He demonstrated the incorporation of radioactive thymidine

one of the nitrogenous bases that are the building blocks of DNA, into a DNA fraction At the same time, Ochoa announced the synthesis of RNA with an Azotobacter enzyme These studies were extended to include the other nitrogenous bases adenine, guanine and cytosine With further purification of the enzyme extracts, Komberg mixed the four bases, a bit of DNA, and the purified enzyme and this synthetic DNA was shown to be identical with native DNA The experiments brought within reach the artificial synthesis of hereditary material and proteins and a full understanding of the mechanisms of genetic and enzymatic control over metabolism and growth

## 1960

BURNET, SIR FRANK M

Nationality Australian
b September 3, 1899, Traralgon, Victoria, Australia d 1985

MEDAWAR, SIR PETER BRIAN

Nationality British
b Feb 28, 1915, Rio de Janeiro d Oct 2, 1987

*For discovery of acquired immunological tolerance*

Burnet was a graduate in medicine from Melbourne (Australia) and spent his entire career there excepting for a brief two year stint with bacteriological research in London His work (1930's) on bacteriophages and a method for culturing some viruses in live chick embryo, led him to the view that an animal s ability to produce antibody in response to an antigen is not inborn, but is developed during foetal life This was supported by Medawar with his ingenious work with mouse skin grafts

Burnet s work also included the mode of action and the epidemiology of influenza virus, polio, Q fever and the cholera vibrio A general scheme explaining how immune systems develop the ability to distinguish between "self and nonself" was proposed by him in 1951 through his clonal selection theory

Medawar the British pioneer in immunological studies was born in Brazil, the son of a Lebanese-British businessman A student of Young at Oxford in 1932, he began his work on skin grafts in connection with wartime burn victims in the 1940 s He continued his work in Birmingham where he moved to in 1947 and was aware of Burnet s work and his suggestion that an animal s ability to produce antibodies against foreign cells is not inherited but is developed in foetal life His demonstration with mouse skin grafts that immunological tolerance is achievable, led to successful human organ transplants in the 1960 s This is achieved by using tissue-typing to secure a partial matching between the donor organ and the patient Immuno-suppressive drugs are then used to inhibit the normal immune response which would cause rejection

## 1961

VON BEKESY, GEORG

Nationality American

b June 3, 1899, Budapest, Hungary, d June 13, 1972, Honolulu

*For his discoveries of the physical mechanism of stimulation within the cochlea*

Bekesy studied chemistry at the University of Bern and did his Ph D in Physics in 1923 from the University of Budapest His work on long distance telephone transmission at the Hungarian Post Office made him interested in the science of audio-reception and the human ear as the major component of the human transmission and receiver system At the Karolinska Institute and the Technical Institute in Sweden, where he moved to in 1946, he designed the new audiometer that can be operated by the patient

The audiometer has applications outside the field of hear
ing also He migrated to America in 1947 and worked in
the psycho acoustic laboratory at Harvard University until
his retirement

1962

CRICK FRANCIS HARRY COMPTON

Nationality British

b June 8 1916 Northampton England

WATSON, JAMES DEWEY

Nationality American

b April 6, 1928 Chicago

*For their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material*

## WILKINS, MAURICE HUGH FREDERICK

Nationality British

b December 15, 1916, Pongaroa, New Zealand

Crick with Watson and Wilkins dominated the so-called dogmatic' era (1950-1965) of biochemical genetics When Watson and Crick began working on the structure of DNA its chemical composition had already been determined The problem was to devise a molecular model that would not only be in agreement with X-ray diffraction data but would also account for the regularity of the molecule s structure, its chemical stability and how the molecule could replicate itself faithfully They had to determine what physical arrangement was possible and search for known molecular forces that could hold the parts of the molecule together

As a result of endless days of building numerous possible structural models of DNA and piecing together essential data obtained from the research of several scientists — including Maurice Wilkins Rosalind Franklin, John Griffith, Erwin Chargaff, Linus Pauling and Jerry Donohue to name only a few — Watson and Crick announced their model of DNA in a short article in *Nature* (1953) Their model consisted of two helices (the double helix) wound around each other, appearing very much like a spiral staircase, with steps composed of paired bases, and with a sugar phosphate backbone spiraling around the outside This model accounted beautifully for the major genetic structural and biochemical aspects of hereditary material On the biochemical and structural level it explained the data obtained from X-ray diffraction studies of DNA and the climbing pattern of bases at regular intervals On a genetic level it explained how the hereditary material duplicated itself and suggested how DNA stores genetic information In short Crick s collaboration with Watson had resulted in the single most important development in biology of the present century The secret of life, that is the nature of the gene had been found out!

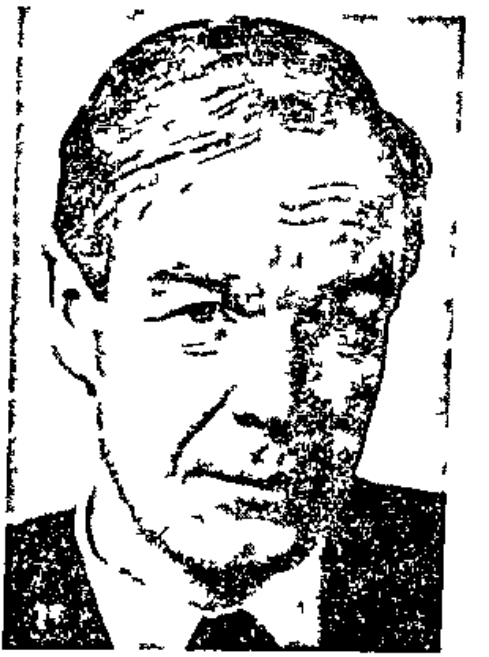
Perhaps the most important contribution to biology made by them was their insistence on relating every structural feature of DNA to the requirements of its biological function In essence they had pulled together the once separate disciplines of classical genetics biochemistry and molecular genetics to form a unified biology

## 1963

ECCLES, SIR JOHN CAREW

Nationality Australian

b January 27, 1903, Melbourne Australia



HODGKIN, SIR ALAN LLOYD

Nationality British

b February 5, 1914, Banbury, Oxfordshire

HUXLEY, SIR ANDREW FIELDING

Nationality British

b November 22, 1917, London

*For their discoveries concerning the ionic mechanisms involved in excitation and inhibition in the peripheral and central portions of the nerve cell membrane*

Eccles, the Australian neurophysiologist was educated at the University of Melbourne and at Magdalene College, Oxford His work at Oxford University and at Canberra showed that the excitement of the nerve cells with impulses results in the release of a substance (probably acetyl choline) in the synapse into the next nerve cell that in tur results in the expanding of the pores in the cell membranes These pores (bontons) allow passage of sodium ions into the neighbouring nerve cell and reverse the polarity of electrical charges Electrical impulses that conduct nerve impulses are thus converted into chemical impulses at the synaptic region and the sequence of the impulses is main tained The excited nerve cells, he found induce another type of synapse to release a substance which promotes out ward passage of positively charged potassium across the membrane By this process the existing polarity of the nerve fibres is reinforced and the transmission of impulses are inhibited

Hodgkin the English neurophysiologist became interested in the basis of nervous conduction even when he was a stu dent of biology and chemistry at Cambridge He found that it was easier to obtain single nerve fibres from a shore crab and even though they were small (1/30 mm diameter), these could be used in experiments

In America (1938) he started using the giant squid (genus *Loligo*) that are half a metre long and highly active with nerve fibres as broad as 1 mm By 1939 Hodgkin along with his student Eccles began the work on squid axon that

continued again in 1945, after their war service Nerve impulse is electrical and a major nerve fibre acts as a cable Hodgkin, Eccles and associates inserted a fine microelectrode into an axon, and placed a second electrode on the outer surface of its surrounding membrane A resting fibre has a negative electrode potential "inside" compared with the positive exterior surface This is reversed during nerve conduction when an impulse passes for about a millisecond and the nerve impulse moves as a wave of depolarisation passing along the axon Hodgkin and Huxley developed a detailed theory of the origin of this membrane potential, relating to the presence of sodium and potassium ions and their distribution across the membrane Their work is basic for the understanding of the biophysics of nervous conduction Hodgkin became President of the Royal Society of London in 1970

Huxley was educated at the University College London and at Cambridge Half-brother of the famous biologist Sir Julian Huxley he was Director of Studies at Trinity College, Cambridge (1952-60) and Professor of Physiology at the University College since 1960 His theories on muscle structure and contraction are widely respected

## 1964

BLOCH KONRAD

Nationality American

b January 21 1912 Neisse Germany now in Poland

LYNEN, FEODOR

Nationality German (FRG)

b April 6 1911, Munich
d 1979

*For their discoveries concerning the mechanism and regulation of cholesterol and fatty acid metabolism*

Bloch obtained his degree in engineering from Munich in 1934 after which he moved to Switzerland and then to the U S A where he obtained his Ph D at Columbia University He became Professor of Biochemistry at Harvard Bloch was especially interested in unsaturated fatty acids and with David Rittenberg discovered that acetic acid was a major building block in the biosynthetic pathways of

cholesterol synthesis. In this he was joined by Lynen and they investigated the mechanism by which acetic acid molecules combine to form smaller and then larger units on the way to the formation of cholesterol.

Lynen studied chemistry at the University of Munich and worked under the Nobel laureate Heinrich Wieland, who was to later become his father-in-law. He was Professor of Biochemistry at Munich (1942-54) and became the Director of Cellular Chemistry at the Max Planck Institute in 1954.

In Wieland's laboratory, Lynen was involved in the work on acetic acid. In his own words, "one of the simplest organic carboxylic acids, containing only two carbons, which occupies a key position in the metabolism of all the living creatures". Starting on the assumption that acetic acid would react faster in the organism than its normal slow rate in the laboratory, he postulated an activated acetic acid in which not only ATP source of energy but also the coenzyme A (discovered by Lipmann) was involved. He succeeded in determining the structure of the activated acetic acid as also the co-enzyme A. This is a tremendous source of energy and the organism, through a series of intermediary steps, is able to synthesize vital substances including cholesterol.

Lynen further studied the oxidation of fatty acids and described its cycle. Their work has contributed to the medicaments of arteriosclerosis, one of the most dangerous of diseases.

Francois Jacob and his colleagues (most notably Jacques Monod) were among a group of molecular biologists who contributed to the revolution in biology during the 1950's and 1960 s with new insights into the biochemistry of life One of these was the concept of "allostery" Literally meaning "other site", this explains that enzyme activity can be controlled by the binding of a chemical structurally unrelated to the substrate to a site other than the active site for that substrate on the enzyme protein Any metabolic pathway could be connected with any other pathway in the cell by this process Allostery explains a wide variety of protein activity control mechanisms including oxygen-haemoglobin binding hormonal control of enzyme activity and even repressor proteins

The genes located along a DNA molecule are present at all times, yet, not all genes on all DNA molecules in a cell function at all times A cell never manufactures the maximum amount of every compound it is capable of producing at all times The amount of any particular substance produced by a cell varies Monod s research on the bacterial enzyme B-galactosidase led him to propose a model in which gene action is regulated by portions of the DNA molecule adjacent to the gene itself The model contains two distinct parts the 'operon' and the regulator gene The operon, in turn, consists of two parts an operator gene and a sequence of structural genes The structural genes are the portions of the DNA molecule responsible for the synthesis of RNA molecules which act as the template for new protein molecules The operator gene is found adjacent to one or more structural genes In most cases studied so far, a single operator gene controls the operation of a series of structural genes which manufacture the enzymes for a sequence of biochemical reactions

How is the operator controlled? Monod and his colleagues suggested that this was the function of a regulator gene, located on the same DNA molecule, but at some distance from the operon This releases a 'repressor" which binds to the operator gene and switches it to an "off position in which the operator gene prevents the structural genes from manufacturing RNA molecules The regulator gene is controlled by cell constituents An excess of certain cell products will cause the regulator gene to release a repressor which turns off the operator gene, while an excess of other cell products will bind to the repressor itself allowing the operator gene to switch to the on position. The basic principles of this theory have now been confirmed

1966

ROUS, PEYTON

Nationality American
b Oct 5 1879, Baltimore Maryland d Feb 16 1970 New York

HUGGINS, CHARLES B

Nationality American
b Sept 22 1901 Halifax Canada

*Rous, for his discovery of tumour inducing viruses, and Huggins, for his discoveries concerning hormonal treatment of parasite cancer*

Huggins was educated at the University of Acadia and the Harvard Medical School He worked in the faculties of the Universities of Michigan and Chicago, and at the Ben May Laboratory for Cancer Research, University of Chicago He demonstrated the possibility of hormonal therapy in cancer by showing that the injection of a synthetic female sex hormone can cause the disappearance of tumours in the prostate glands of the male

After obtaining his medical degree from Johns Hopkins University, Rous shifted to the Rockefeller Institute in New York where he started his sixty year long research on cancer A tumour occurring naturally in fowl was successfully transplanted by cell grafts, in series Rous, then demonstrated that this transplantation could be done through cell free filtrates also He went on to show that the tumour differed in no way from known tumours except in having a demonstrable cause and that the filterable agent had properties like those of known viruses In the 1930 s Rous borrowed virus induced warts in cottontail rabbits from R E Shape and demonstrated the changes that take place when a single wart acquired the properties of a malignant growth It was shown that the virus and carcinogenic chemicals could act synergistically, cancer being caused by their combined action faster than by either agent acting alone Rous s proposal that carcinogenesis involved two processes, initiation and promotion, that carcinogenic agents act in one way or the other, or both ways, is now generally accepted The filterable foul tumour bears his name, Rous Sarcoma Virus (RSV)

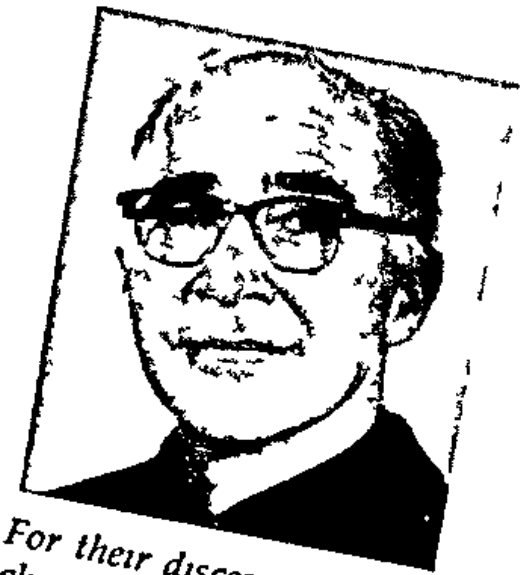
## 1967

GRANIT, RAGNAR

Nationality Swedish
b October 30 1900
Helsinki

HARTLINE, HALDAN KEFFER

Nationality American
b December 22 1903
Bloomsburg Pennsylvania



WALD, GEORGE

Nationality American
b November 18 1906
New York

*For their discoveries concerning the primary physiological and chemical visual processes in the eye*

The Swedish neurophysiologist Granit graduated from Helsinki University in 1927 After training in medical physics at the University of Pennsylvania, he trained in neurophysiology under Sherrington (Nobel laureate) at Oxford He returned to Sweden in 1940 and joined the Royal Caroline Institute of Stockholm and became its Director in 1945

The American neurophysiologist Hartline took his graduate degree from Lafayette College and his M D from Johns Hopkins University (1927) After training in medical physics in Munich, he returned to America where he became Professor of Biophysics at Johns Hopkins University

The biochemist Wald was educated in New York and Columbia Universities and did his Ph D in 1932 after which he joined Harvard University where he became a Professor of Biology in 1948

These three researchers were interested in the physiology and chemistry of visual processes and contributed significantly to the development of this area of science Granit demonstrated (1945) that single nerve fibres from the retina were differentially sensitive to different wavelengths of light Hartline was the first neurophysiologist to record the activity of a single visual receptor He devised techniques for intercepting and recording the electrical signal sent by an isolated single nerve fibre where receptors are stimulated by light

Wald studied the activation of the photoreceptor cells in the retina by light and the molecular readjustments that take place as a result These chemical processes were reproduced by him in the laboratory

## 1968

**HOLLEY ROBERT W**

Nationality American
b January 28 1922
Urbana Illinois

**KHORANA, HAR GOBIND**

Nationality American
b January 9, 1922, Raipura
Punjab India (now in
Pakistan)

**NIRENBERG, MARSHALL W**

Nationality American
b April 10 1927, New
York City

*For their interpretation of the genetic code and its function in protein synthesis*

Holley graduated in Chemistry from Illinois University (1942) and obtained his Ph D from Cornell University (1947) At the California Institute of Technology (Caltech) which was a nerve centre of molecular biology, he formed his basic concepts and strategies and realised that isolation of pure molecules of transfer RNAs was a prerequisite for understanding the function of nucleic acids At Cornell, to which he returned, he and his team spent three years isolating one gram of alanine transfer RNA from some 90 kilograms of yeast The genetic material DNA communicates to the cells through messenger RNAs which transfer the messages to the transfer RNAs for further actions Holley and his group worked out the complete sequence of nucleotides (77 in all) in the amino acid alanine, by 1965

The Indian American molecular biologist Khorana was educated at the Universities of Punjab, Liverpool (Ph D in Chemistry in 1948), Zurich and Cambridge At Vancouver, where he moved in 1952, he extended his study of the synthesis of nucleotide coenzymes At Wisconsin (1960-1970), he carried out the synthesis of polynucleotides with known base sequences His work was of tremendous importance in establishing the "genetic code word dictionary The four bases adenine thymine, guanine and cytosine (A T G and C) present in DNA chains are 'read' sequentially in group of three 'codons' This sequence was known to be "non overlapping" and "commaless' Since there are 21 known amino acids and 4 bases, the coding was to be in the form of a triplet (ATC AAA, etc) — $4^3 = 64$ combinations as, otherwise, there would be overlapping In triplets, however, there would be some codons that would code for more than one amino acid and some that are 'nonsensical' Khorana synthesized all the 64 codons and his work is of major significance in molecular biology

Nirenberg studied Zoology for his Masters (1952) and did his Ph D in Biochemistry (1957) from the University of Florida He played a major role in the study of the genetic process of protein synthesis The double stranded DNA un winds itself at the time of protein synthesis and through the single stranded RNA that it synthesizes, transfers the messages and codes for the amino acid sequences in the protein molecule through the messenger RNAs (m RNA the sites of the synthesis, the ribosomes Nirenb demonstrated the steps that link DNA, RNA and protei showing that RNA is a prerequisite for protein synthesis

1969

DELBRUCK, MAX

Nationality American

b September 4 1906 Ber lin Germany d March 10 1981

HERSHEY, ALFRED D

Nationality American

b December 4 1908 Owosso Michigan

## LURIA, SALVADOR EDWARD

Nationality American
b August 13, 1912, Turin, Italy

*For their discoveries concerning the replication mechanism and the genetic structure of viruses*

Delbruck a student of physicist Niels Bohr, was schooled in the mathematical examination of natural phenomenon He chose bacterial viruses (bacteriophage) as an experimental system The life cycle of the bacteriophage was obscure, with conflicting data from different phage strains and bacterial host species Delbruck limited the choice to the virulent T phage strains that infect the human gut bacterium *Escherichia coli*, and suggested standardizing growth temperature and medium As a result, much progress was made concerning the sequence of events that characterize a phage infection and successful production of progeny

These studies defined an "eclipse period immediately fol
lowing the phage infection during which no progeny c
be detected, and the infected unit took on the cha
teristics of the host cell Extension of this 'latent perc
before the first appearance of progeny was shown
Delbruck in 1940 to result in an increase in the yield
total progeny The characteristic size of the phage particle
of each of several strains was shown to be independent of
the yield of progeny Heritable variants or mutants of
viruses were discovered in the mid-1940 s and co-infection
of E coli by mutationally marked phage parents led to a
genetic map of phage genes

Luria s collaboration with Max Delbruck (results published
in 1943) had an enormous impact, because this study
demonstrated that bacterial variants ' were in fact
mutants and the origin of such variants corresponded
quantitatively to mutational processes in the higher or
ganisms studied by classical geneticists

Hershey's contributed to the understanding of phage mul
tiplication At the Cold Spring Laboratory U.S Hershey,
with Martha Chase studied phage entry into bacterium
with labelled radioactive materials The bacteriophage par
ticle thrust its pointed tail into the wall of a bacterium and
shot its contents into the interior of that cell Whereas the
emptied coat of the phage remained outside like an empty
syringe the bacterium after twenty four minutes, burst
open exposing hundreds of carbon copies of the invade
viruses The infected material had taken control of the cell
and used the cell s content to produce new viruses of its
own kind Hershey and his colleague demonstrated that it
was DNA that was squirted by the phage into the bac
terium and by inference, DNA was the genetic material

1970

ELROD, JULIUS

:ionality American
May 30 1912, New York

KATZ, SIR BERNARD

Nationality British
b March 26, 1911, Leipzig

VON EULER, ULF

Nationality Swedish
b February 7, 1905, Stockholm d March 12, 1983, Stockholm

*lieir discoveries concerning the humoral transmitters in the terminals and the mechanism for their storage, release and vation*

Axelrod the American neurophysiologist, had to struggle against grave economical odds before he could become a full time researcher He had considerable experience in enzyme physiology and had discovered enzymes in the liver microsome which are involved in the metabolism of drugs. He obtained his Ph D from the George Washington University in 1955 at the age of 43 He studied the biosynthesis of metabolism in the pineal body and established that this is a neurochemical transducer and not a function less structure as was envisaged at that time (1957)

British physiologist Katz was of German origin and graduated from the University of Leipzig (1934) before emigrating to London, where he obtained his D Sc (1943) at the University of London He studied development of sensory terminals and the initiation of impulses in the muscle fibre He also worked on the nature of nerve impulse neural transmitter substances and the release of them in the excitation process

Son of the Nobel laureate in Chemistry (1929) Hans Von Euler-Chelpin the Swedish physiologist Euler was a student and later professor at the Royal Caroline Institute in Stockholm Nerve transmission had been shown to be at least partly chemical by T R Elliott as early as 1903 Later Dale and O Loeui and, in 1946 Euler, isolated neurotransmitter of the sympathetic nervous system and showed it to be non-adrenalin and not adrenalin as originally envisaged Euler's earlier work (1935) on human semen where he demonstrated that human semen contained a potent chemical which lowered blood pressure and contracted muscle — he named it prostaglandin" — had initiated another important area of research in biochemistry

1971

## SUTHERLAND, EARL W JR

Nationality American
b November 19, 1915, Burlingame, Kansas, d March 9, 1974, Miami, Florida

*For his discoveries concerning the mechanism of the action of hormones*

Sutherland, American physiologist and pharmacologist, graduated from Kansas (1937) and took his M D from Washington University Medical School, St Louis (1942) Later, he joined the department of Medicine University of Cleveland, Ohio From 1973 he was at the University of Miami Medical School His major area of interest was hormones The isolation by him of cyclic adenosine monophosphate (cyclic AMP) and demonstration of its involvement in various metabolic processes that occur in animals was a major breakthrough in hormonal chemistry

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## 1972

EDELMAN, GERALD MAURICE

Nationality American
b July 1 1929, New York.

PORTER, RODNEY ROBERT

Nationality British
b October 8 1917, Liverpool, d September 8, 1985

*For their discoveries concerning the chemical structure of antibodies*

The American biochemist Edelman began investigations into immunoglobins as a doctorate student at Rockefeller University and continued the work when he joined the faculty Antibodies form a class of closely related proteins, each specific in its ability to bind with a specific antigen and this system forms a major part of the defence mechanisms of vertebrates against infection Edelman discovered that human immunoglobin, a large protein

molecule, is a combination of two — light' and 'heavy" — protein chains linked by sulphur bridges By 1969 he showed that 1330 amino acids form a Y-shaped structure in the chains of the immunoglobin IgG Further, he showed that the amino acids in the tips are variable but the main part of the structure is constant

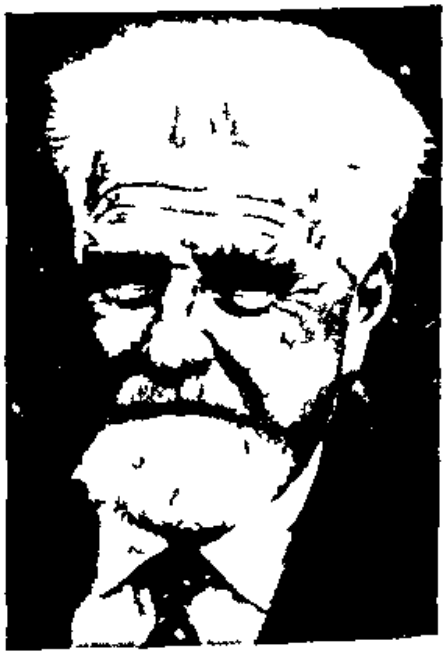
The British biochemist Porter was educated in Liverpool and, after a military career during World War II, worked on proteins at Cambridge with Sanger, the two-time Nobel laureate In 1950, Porter demonstrated that antibodies could be partly broken down without total loss of their antigen-binding ability By 1960 he could show that they contain both 'heavy" and light" protein chains and that they have three distinct regions of which two are alike and serve to bind antigens Using Edelman's results as also data from electron microscopy, Porter brilliantly guessed the overall molecular structure of the antibodies

Further work by Milstein (Nobel laureate, 1984) and others have refined the structural understanding further The missing link of the structure of antibodies, begun by Ehrlich (Nobel laureate, 1908), was developed by Landsteiner (Nobel laureate, 1930) Pauling (Nobel laureate, 1954) and solved by Porter (1972) Porter was killed in a road accident in 1985

## 1973

**VON FRISCH, KARL RITTER**

Nationality German (FRG)
b November 20, 1886, Vienna, Austria d June 12 1982 Munich



**LORENZ, KONRAD ZACHARIAS**

Nationality Austrian
b November 7, 1903, Vienna, d February 27, 1989, Altenberg Austria

**TINBERGEN, NIKOLAAS**

Nationality British
b April 15, 1907, The Hague

*For their discoveries concerning organization and elicitation of individual and social behaviour patterns*

Von Frisch set out to prove bees were capable of distinguishing colour His experiments not only confirmed this but also demonstrated that bees see ultraviolet (UV) light as a separate colour, a colour to which we are blind Von Frisch discovered the language of the bee For more than 2000 years man had known that if food is placed near a beehive it might go unnoticed for days but when discovered many more bees soon arrive The first bee to find the food has been called a "forager' and the ones to come later, "recruits' Von Frisch's initial observations suggested that foragers performed two types of dances in the hive to attract recruits, one a round dance implying sugar was available and the other a figure-eight or waggle dance when pollen was in the area of the hive This interpretation remained unchallenged for over 20 years when Von Frisch, himself, unravelled the true secret behind the language of the bee His careful experiments determined that the round dance actually meant food was nearby and the waggle dance that food was at some distance More remarkably, Von Frisch found that the duration of the waggle dance indicated distance to the food and the straight portion of the dance direction On a vertical hive, "straight up' corresponded to the direction of the sun The angle of the straight portion of the waggle dance from the 'straight up' direction of the dance indicated the angle of the food source from the sun

Konrad Lorenz applied the accepted methods of observation and objective description used in anatomy and physiology to the world of animal behaviour Before the 1930's animal behaviour was studied either by experiments under conditions unrelated to the animal s natural environment or through field studies of one species, with no attempt at establishing rules and laws that govern behaviour

In the late 1930 s Lorenz and Nikolaas Tinbergen wrote a series of theoretical papers laying the foundation for modern ethology Perhaps the most famous is on the egg retrieval response in the greylag goose Lorenz and Tinbergen described how a brooding goose will retrieve an egg that has rolled out of its nest The goose rises, extends its neck, places its bill over the egg and rolls the egg back into the nest The "motor program" is innate, highly stereotyped, and will continue to completion even if the egg is removed from under the bill in mid journey They called the goose's behaviour a ' fixed action pattern ' (FAP) Triggering the FAP they hypothesized an "innate releasing mechanism' (IRM) within the animal which acts in response to stimuli or releases" from the environment. Because only one aspect of the stimulus leads to a response, the term 'sign-stimulus" is often used

Lorenz discovered a dramatic example of programmed learning imprinting Orphaned geese or ducks under two days old would follow Lorenz as if he was their parent This parental imprinting' was a rapid and relatively irreversible learning process during an optimal "critical' or sensitive' period Furthermore when the geese became adults they would court humans instead of other geese Not until Lorenz made his contribution did the study of behaviour gain momentum, a momentum which it has not since lost

Tinbergen along with Lorenz is well known for his field observations of animals in actual habitats His consistent and long study of seagulls led to significant generalizations of mating behaviour and courtship His younger brother, Jan Tinbergen is the recipient of the 1969 Nobel Prize in Economics

## 1974

**CLAUDE, ALBERT**

Nationality Belgian
b 1899 Langier, Belgium
d May, 1983

**DE DUVE, CHRISTIAN RENI**

Nationality Belgian
b October 2 1971
Thames-Ditton, England

**PALADE, GEORGE EMIL**

Nationality American
b November 19, 1912,
Jassy, Romania

*For their discoveries concerning the structural and functional organization of the cell*

The Belgian cytologist Claude graduated in Medicine from the University of Liegi, Belgium, and was with the Rock efeller University, New York for over two decades before he shifted to Lonvian He was one of the pioneers in the use of electron microscopy for cellular studies His work on the isolation of cellular components contributed remarkably to the work of De Duve and Palade, who shared the Nobel Prize with him

De Duve was educated in medicine at the Catholic Univer sity of Lonvian and worked in Sweden and the U S before returning to Lonvian in 1947, he later held a dual post also at the Rockefeller University, New York. His discovery of small organelles — lysosomes — with the help of the electron microscope in 1955 was a major breakthrough in the study of digestive enzymes As early as 1949, he had collected convincing evidence to indicate that at least some of the digestive enzymes must be enclosed within smaller organelles in the cytoplasm of cells The packaging of en zymes in membranous enclosures in the form of lysosomes serves both to isolate the enzymes from attack on their own animal or plant cells and also to concentrate their attack when the lysosome fuses with a food vacuole The macro molecules of the food are digested and the resulting small molecules of sugar or amino acids are passed through the lysosome wall into the cell Absence of lysosomal enzyme results in hereditary metabolic diseases like cytinosis De Duve has also done important work on cancer

Palade qualified at Bucharest, Romania in Medicine in 1940 He moved to the U S in 1945, working first at the Rockefeller Institute in New York and from 1972 at Yale His work with the help of the electron microscope revealed that mitochondria are the sites where energy is generated

by enzymatic oxidation Mitochondria, the sausage-shaped organelles of the cytoplasm in animal cells, cluster the endoplasmic reticulum and are storehouses of energy, in the form of adenosine triphosphate (ATP), which is required by the cells for their metabolic activity Palade discovered smaller organelles called ribosomes which are rich in ribonucleic acid (RNA) and showed that they are the sites of protein synthesis His further work was on the pathway followed by secretory proteins in glandular cells He also worked on blood capillaries and the transport of essential life-supporting materials through the capillary walls

## 1975

BALTIMORE, DAVID

Nationality American

b March 7, 1938, New York City

DULBECCO, RENATO

Nationality American

b February 22, 1914, Cantanzaro, Italy

## TEMIN, HOWARD MARTIN

Nationality American
b December 10, 1934, Philadelphia

*For their discoveries concerning the interaction between tumour viruses and the genetic material of the cell*

Baltimore studied chemistry at Swarthmore and did his post-graduation at the Massachusetts Institute of Technol ogy and his Ph D at Rockefeller University In 1972 he became Professor at MIT and later director of the Whitehead Institute, Massachusetts His work in 1968 on the replica tion of the polio virus wherein the RNA of the virus first constructed a polyprotein which then split into a number of protein molecules, was a major step in the under standing of viral replication Out of the smaller protein molecules, two polymerised RNA, whereas the others formed the protein coat of the new viral particles

Baltimore and Temin each independently discovered the enzyme "reverse transcriptase", for they were awarded the Nobel prize Reverse transcriptase modified the "central dogma ' of molecular biology wherein the chain was supposed to be DNA—RNA—Protein, in which the first arrow is *transcription* and the second, *translation* These were assumed to be unidirectional processes until the discovery of reverse transcriptase, which was shown to be able to transcribe RNA to DNA

Dulbecco studied medicine at Torino University and obtained his M D in 1936 After a stint in the army he joined Luria in Bloomington, Indiana Between 1952 and 1963, he was at Caltech after which he joined the Salk Institute His major contribution was his setting up experiments to study the processes by which normal cells become cancerous He introduced the concept of cell transformation

Temin studied biology at Swarthmore and obtained his Ph.D in Virology at Caltech in 1959 From 1960, he was with the University of Wisconsin

His discovery, in the early 1960 s, that Rous Sarcoma Virus (RSV) is inhibited in its replication in the presence of the antibiotic actinomycin D, started the search for the enzyme reverse transcriptase Unlike as in the central dogma (DNA—RNA—Protein), RNA RSV replicated through a DNA intermediate He called this DNA the "Provirus ' Temin realized the significance of this work and proposed RNA (of the RSV) — DNA (provirus) — RNA (replicated RSV) In 1970 Temin identified the enzyme reverse transcriptase, which was also individually done by Baltimore

## 1976

**BLUMBERG, BARUCH SAMUEL**

Nationality American
b July 28, 1925, New York City

**GAJDUSEK, D CARLETON**

Nationality American
b September 9, 1923, Yonkers, New York

*For their discoveries concerning new mechanisms for the origin and dissemination of infectious diseases*

Blumberg the American physician, graduated from Union College (1946), completed his M D from Columbia University College of Physicians and Surgeons (1951) and his Ph D in Biochemistry from Oxford He travelled extensively in East and West, his contribution to geographic medicine is significant His work on Hepatitis B and its prevention is well known His discovery of the cause of the disease 'kuru seen amongst a cannibalistic tribal group in New Guinea, fetched him the Nobel Prize

Gajdusek was educated in physics at Rochester and in medicine at Harvard before working with Pauling at Cal-Tech, and later in Iran and in Papua New Guinea among the Fore people here he observed, as did Blumberg, that they often die from a viral disease called "kuru' The disease seemed to be specific to females and is assumed to be caused by eating the brains of the dead Gajdusek showed that it could be passed to other primates like chimpanzees, but the infection took more than 12 months to develop A lot of other diseases like herpes, "cold sore', have been shown to be due to slow and persistent viral infections "Kuru' is the first such recorded viral infection disease

1977

GUILLEMIN, ROGER CHARLES LOUIS

Nationality American
b January 11, 1924, Dijon, France.

SCHALLY, ANDREW VICTOR

Nationality American
b November 30, 1926 Wilno, Poland (Now Vilnius, Russia)

*For their discoveries concerning the peptide hormone production of the brain*

Guillemin, the French biochemist, works at the Salk Institute of Biological Studies, San Diego, California Schally, the Polish-American biochemist, fled his native Poland to Britain in 1939 Later, he shifted to America, to the Baylor College of Medicine, Houston, Texas where Guilleman asked him to join him on a project on hormonal chemistry Their initial work was the isolation of the substance that regulated the secretion of Adrenal Corticotropic Hormone (ACTH) They did succeed in isolating the hormone, but independent of each other, and it was named the "thyrotropic hormone releasing factor" Their major work, however, was the demonstration that concentration of other hormones secreted by the hypothalamus was a prerequisite for the secretion of the pituitary gland

YALOW, ROSALYN

Nationality: American

b July 19, 1921, Bronx, New York.

*For the development of radio immuno assays of peptide hormones*

The American nuclear physicist Yalow has a special interest in radioisotopes and turned to nuclear medicine from 1972 as a staff of the Bronx Veterans Administration Hospital and the Mount Sinai School of Medicine, New York City. After two decades of work along with her colleagues Solomon Berson, she developed the method of radio-immuno-assay to detect and measure peptide hormones (such as insulin) in the blood. Radio immuno-assay is an extremely sensitive and specific technique used for measuring the concentration of various biologically active substances that are present in the human body in such infinitesimal quantities, that so far they were practically undetectable by any methods of assay. She found that the immune system of the individual produces an antibody against insulin which neutralises the foreign proteins.

The method has to be of immense value in locating the origin of the hormones in the body. It is also useful in the clinical diagnosis and treatment of a variety of diseases and of male and female infertility. The potential value of the method is so enormous since it can be used to measure very small amounts ($10^{-12}$g) of any substance that requires an antibody. Improvement of this technique has already led to better control of digoxin therapy in heart diseases, and diagnosis of neural crest diseases like *spina bifida*.

1978

ARBER, WERNER

Nationality Swiss
b 1929, Granichen, Switzerland

NATHANS, DANIEL

Nationality American
b October 30, 1928, Wilmington, Delaware

SMITH, HAMILTON OTHANEL

Nationality American
b August 23, 1931, New York City

*For the discovery of restriction enzymes and their application to problems of molecular genetics*

Arber studied at the Universities of Geneva and Southern California before teaching at Geneva University (1960-1970), as Professor of Microbiology Since 1970, he heads the microbiology department at the University of Basel His follow up work on the phenomenon of host induced variation discovered by Luria contributed further knowledge to the field of "restriction enzymes' These are protective enzymes present in bacterium that modified the DNA of infesting viruses His hypothesis to explain the phenomenon of host controlled variation in phages was confirmed by Smith (1970), who identified the enzyme and extracted it from the bacterium *themophilus influenzae* (Hind II)

Hamilton Smith graduated in mathematics in 1952 and in medicine in 1956 from Johns Hopkins University where in 1973, he became Professor of Microbiology He confirmed and amplified the earlier discovery of the restriction enzyme of Arber that was obtained from *E Coli* bacterium (1960) The Hind II enzyme of Smith cleaved DNA at specific sites in relation to the sequence of bases in DNA Smith and other workers, especially D Nathans (who col laborated with Smith in some of the research) isolated many such enzymes

Daniel Nathans studied at the University of Delaware and at Washington, St Louis, Missouri, before joining the faculty of Johns Hopkins University in 1967 He recognized the significance of the restriction enzymes in cleaving the DNA of the simian virus (SV40) and demonstrated (1971) that the enzyme discovered by Smith could split the DNA molecule of SV40 virus into 11 clearly defined fragments By using two more enzymes he broke the SV40 virus DNA molecule further and mapped the genetic construction of the virus completely

1979

CORMACK, ALLAN MACLEOD

Nationality American

b February 23, 1924, Johannesburg, South Africa

HOUNSFIELD, GODFREY NEWBOLD

Nationality British

b August 28, 1919, Newark, England

*For the development of computer assisted tomography*

Cormack, the South African physicist, had his early educa tion at the University of Cape Town and then worked on the medical applications of radio isotopes in Johannesburg While on a prolonged convalescence in a South African hospital, he realised that X rays were used only for obtain ing two-dimensional "silhouettes', primarily of bone struc ture In 1956 he migrated to America and later became a Professor of Physics at Tufts University, Massachusetts

In 1963, he proposed a mathematical basis by effectively combining many X-ray images taken in different directions through the human body, to build up a picture of a slice through the tissue. Named Computer-assisted tomography (CAT), this technique is the basis for the modern body scanners built by Hounsfield in the early 1970 s.

The British physicist Hounsfield studied at the City and Guild's College and at the Faraday House College for Electrical Engineering in London. With his previous experience in solid state computers, he joined EMI (Electrical Musical Industries), becoming head of the medical research division

Independent of Cormack, he conceptualised the design of CAT between 1969 and 1972 and the actual scanner for the complete human body was developed by 1974 High-resolution images of the soft body tissues (which are normally almost transparent to X rays) are built up by computer from innumerable measurements of the absorption of X ray beams in different directions through the body CAT scanning has revolutionised the field of nuclear medicine Hounsfield is a leader in the field of medical imaging particularly the use of nuclear magnetic resonance (NMR) techniques

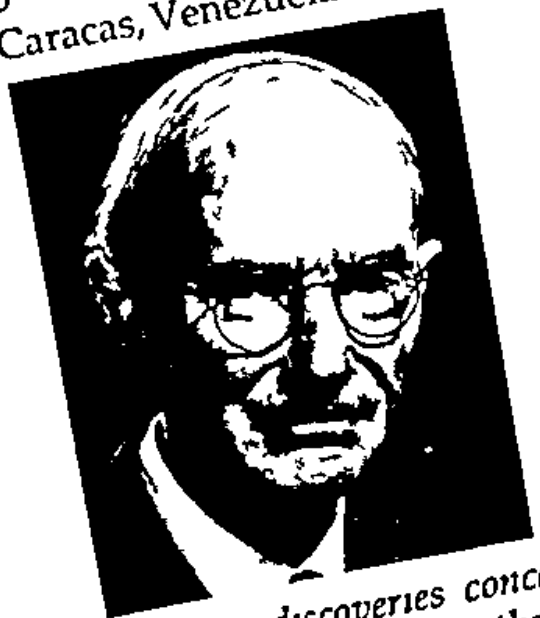
1980

BENACERRAF, BARUJ

Nationality American
b October 29, 1920,
Caracas, Venezuela

DAUSSET, JEAN

Nationality American
b October 19, 1916,
Toulouse, France



SNELL, GEORGE D

Nationality American
b December 19, 1903,
Bradford, Massachusetts

*For their discoveries concerning genetically determined struc tures on the cell surface that regulate immunological reactions*

Benacerraf completed his M D (1945) from the University of Virginia, after migrating to America in 1940 After spending time in Paris (1950-1956) and New York Medical School, he moved to the Department of Pathology at Harvard in 1970 as its Professor George Snell had reported that the success of transplants improved when donors were found to be having antigens that were more akin to that of the recipients Benacerraf, while working with guinea pigs, developed on this idea and discovered the Ir (immune response) genes of the H-2 segment as playing a crucial role in the immune system

Dausset, a scientist at St Louis Hospital, Paris University, was, since World War II, interested in transfusion reactions By the 1950 s, he disproved the universal donor status of the O blood group and showed that if the donor has recently been given anti-diphtheria or anti tetanus vaccine, the resulting antibodies can produce shock reactions when the blood is transfused Patients with a history of many blood transfusions were shown by him to be prone to produce antibodies against the white cells He suggested that the antigen HLA (human lymphocyte antigen) is related to the mouse H-2 system Tissue typing', as the work is known, has reduced the rejection risks during transplants considerably and is a major landmark in the development of organ transplant

George Snell, a retired scientist at the Jackson Laboratory, Maine, USA, worked independently on the group of genes that coordinate the body's immune system He proposed the concept of a group of genes — 'Major histocompatibility genes — that were the prime factor in the acceptance or rejection of a tissue graft

## 1981

HUBEL, DAVID HUNTER

Nationality American
b February 27, 1926, Windsor, Ontario, Canada

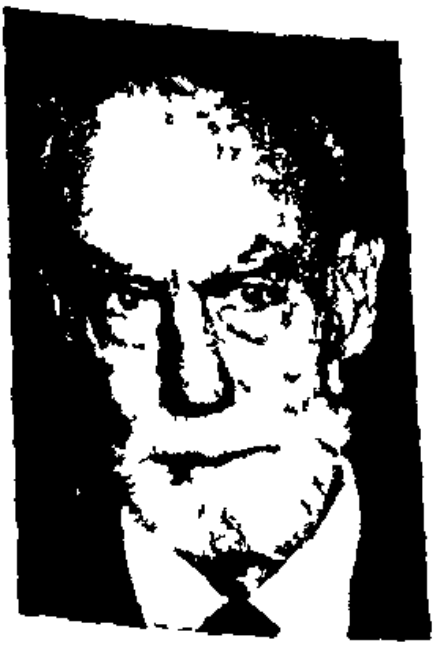
WIESEL, TORSTEN N

Nationality Swedish
b 1924, Uppsala, Sweden

*For their discoveries concerning information processing in the visual system*

Hubel qualified in Medicine at McGill University and in 1959, became Professor at the Harvard Medical School Along with Wiesel, Hubel demonstrated the existence of a decoding system from the retina to the brain that provides a new model for the functioning of the brain They used microelectrodes and modern electronics to detect the activities of the individual neurons, especially in area 17 of the visual cortex This study aided the understanding of the mechanics of visual perception at the cortical level The

cells of this striate cortex lie in many layers arranged in columns which run through the thickness of the cortex (a few millimetres) Hubel and Wiesel found that stimulation of cells on the retina by light causes excitation and specific stimulation in the cortex. The visual stimulation suggests that whereas some cells respond to spots of light, others do so to a line whose tilt is so critical that even a change of 10° in its angle greatly alters the response A few would respond to specific directions of movement or specific colours only Their study has made the visual cortex one of the best known parts of the brain. Wiesel, the Swedish physiologist worked at Harvard University with Hubel With Hubel, he further established that many of these specific response patterns are already present at the time of birth and could be modified or even destroyed by the deprivation of vision in young animals Congenital cataracts and strabismus (squint) treatment have been greatly influenced by these discoveries



SPERRY, ROGER W

Nationality American b August 20, 1913, Hartford, Connecticut

*For his discoveries concerning the functional specialization of the cerebral hemispheres*

The American neurobiologist Sperry was a student of psychology at Oberlin College and of Zoology at Chicago and worked in several centres before finally joining the California Institute of Technology in 1954 as a Professor of Psychobiology His three decades of research have revolutionised the theories of brain function and form the theoretical basis of today's research into the information processing phenomena of the brain

Sperry studied regeneration of optic nerves in amphibians and found that even with obstacles in the path, an amphibian could regenerate a new nerve that would find its way to its original synaptic connection in the brain Working with amphibians, salamanders and higher animals, he demonstrated that both the halves of the brain could be taught to perform similar tasks and each of them possessed independent ability to learn His work on split brain patients (human patients are at times commissarotomised to prevent severe epilepsy spreading) showed that although they are normal in many ways, the right hemisphere of the brain specialises in non verbal processes (like emotions) while the left is dominant in language processing His work suggests the existence of discrete pathways in the brain carrying specific type of information

## 1982

**BERGSTROM, SUNEK**

Nationality Swedish
b January 19, 1916, Stockholm Sweden

**SAMUELSSON, BENGT I**

Nationality Swedish
b May 21 1934, Halmstadt, Sweden

**VANE, SIR JOHN R**

Nationality British
b March 29, 1927 Worcestershire, England

*For their discoveries concerning prostaglandins and related biologically active substances*

Bergstrom was educated at the Royal Caroline Institute in Stockholm and returned there as Professor of Biochemistry in 1958 and is associated with the World Health Organization His interest in prostaglandins, a group of related compounds whose biological effects were first noted in the 1930 s, led to his isolating two prostaglandins, in pure form, in the 1950 s His pioneering work led to isolation of more akin substances like thramboxane, prostacyclin and leukotrienes and the study of their structure by Bergstrom, Samuelsson and John Vane

These are potent chemical transmitters of intra- and inter cellular signals that mediate a variety of physiological functions Their effects are complex and a common feature is their ability to contract smooth muscle and their high potency Originally found in human semen, they have subsequently been isolated in many sources, including the Caribbean sea whip coral Their structure was shown to be of a general pattern of a five-carbon ring with chains of adjacent carbon atoms

Samuelsson Professor of Chemistry and Dean of the Karolinska Institute, contributed significantly to elucidation of the mechanisms of biosynthesis of prostaglandins and the pathways of their metabolism He also worked specially on the synthesis and structure of leukotrienes Much of medicinal chemistry is devoted to the study of prostaglandins and related biologically active substances

John Vane Group Research and Development Director of the Wellcome Foundation in Beckenham, England, is recognised for his discovery of prostacyclin the potent inhibitor of platelet aggregation that is produced by the vascular endothelium

1983

## McCLINTOCK, BARBARA

Nationality American
b 1902, Connecticut

*For her discovery of mobile genetic elements*

McClintock studied at Cornell University and secured her Ph D in plant genetics in 1927 She spent time at Caltech, Freiburg and Missouri then returned to teach at Cornell Her work begun in the 1940's at Cold Spring Harbor Laboratory, was unrecognized until the Nobel Committee hailed it as 'one of the two great discoveries of our times in genetics She was the first woman to win an unshared Nobel Prize for Physiology or Medicine Her work on the coloured kernel in maize led her to conclude that the function of some genes is to control other genes and that some of them move on the chromosome so as to control other genes The concept of 'jumping genes' as proposed and

demonstrated by her must involve the physical movement of DNA from site to site She proposed that characteristics like the colour of kernel can be turned on or off as the case may be by genetic elements that act as switches that can move from one end to the other of the chromosomes

1984

JERNE, NIELS KAJ

Nationality Danish
b December 23, 1911
London.

KOHLER, GEORGES J F

Nationality German (FRG)
b 1946

*For theories concerning the specificity in development and control of the immune system and the discovery of the principle for production of monoclonal antibodies*

MILSTEIN, CESAR

Nationality British/Argentinean
b October 8, 1927, Bahia Blanca, Argentina

The immunological system in the human body consists of a wide variety of cells which adopt different tactics to fight foreign bodies One of these is through the production of antibodies, which is brought about by the lymphocytes Since each type of antibody reacts to a specific "trigger" (antigen), the body has to stock millions of antibody forms Encounter with the foreign body stimulates the cells, which in turn manufacture the specific antibody required Niels Kaj Jerne, along with Cesar Milstein and Georges Kohler, played a decisive role in the clarification of these processes and the complex organisation of the immunological system The breeding of immune cells which manufactur antibodies in nutrient cultures seemed impossible

In 1975, Kohler and Milstein, working in the British Medical Research Council Laboratory for Molecular Biology in Cambridge, decided to use the natural immortal cells — myeloma cells, a certain type of tumour cells — for their research They fused a myeloma cell with an antibody producing lymphocyte from the spleen of a mouse The result was a cell which could be reproduced in the laboratory into a cluster of immortal cells (clones) and which manufactured antibodies Any number of such 'monoclonal antibodies" can be produced They are being used in highly sensitive pregnancy, cancer and AIDS tests and in genetic engineering

1985

BROWN, MICHAEL

Nationality American
b 1941

GOLDSTEIN, JOSEPH LEONARD

Nationality American
b April 18, 1940, Sumter, South Carolina

*For their discoveries concerning the regulation of cholesterol metabolism*

Brown hails from New York and Goldstein from North Carolina, both work at the Health Science Centre of Dallas, University of Texas The two worked on the low-density lipoprotein (LDP) receptor, a molecule that ferries cholesterol rich particles from the bloodstream into the cell The discovery has contributed significantly to the know ledge of cholesterol metabolism and certain cardio vascular diseases We now understand the mechanism through which diet and exercise can help prevent a heart attack

Brown and Goldstein, while investigating a rare inherited disorder hypercholosterolemia, a disease where children have six to ten times the blood cholesterol level and can die of heart attack even as early as age two, compared skin cells of the victims to that of normal people They traced the disease to the absence of LDP receptors, protein that stud the outer membranes of the cells, especially that of the liver Further investigations led to the deciphering of the complex minuet between the receptor and its LDP particle

The body needs cholesterol for manufacturing new cell membranes like acids and steroid hormones Cholesterols are obtained through the food or are made in the liver, and they travel in the bloodstream in the form of lipoproteins round bundles of fat and protein Vacant LDP receptors snare the passing packets of lipoprotein freeing the cholesterol for use Eating of too many saturated fats results in suppression of the production of LDP receptors by the liver cells This in turn leads to atherosclerosis, or accumulation of cholesterol in the walls of the artery A low-cholesterol diet sets off the reverse process

1986

COHEN, STANLEY

Nationality American
b November 17, 1922, Brooklyn, New York City

LEVI-MONTALCINI, RITA

Nationality Italian/ American
b 1909, Turin, Italy

*For their discoveries of growth factors*

Levi Montalcini and Stanley Cohen, who met in St Louis in 1953 at Washington University, found the first of the body s many "growth factors" proteins that guide the development of immature cells From her earliest experiments, Levi-Montalcini, who holds both Italian and American citizenship, focused on the nervous system Before her discovery, scientists did not understand how organs signalled developing nerve cells to link up with them It was Levi Montalcini who first suggested in 1951 that the signal might come from a growth stimulating chemical in

the cells targeted by the nerves This was confirmed in 1952 when she observed that single nerve cells, taken from chick embryos and cultured with tissue from mouse tumours, sprouted nerve fibres that reached out 'like the rays of the sun' Her conclusion there was a growth factor in the tumour tissue Subsequent experiments showed that the mysterious substance was also present in snake venom and mouse salivary glands It was left to Cohen to extract the first pure samples of the protein now known as nerve growth factor Later, working separately, Cohen discovered the epidermal growth factor, which governs cell development in the skin He also located a protein on the surfaces of cells that act as receptors for EGF

1987

TONEGAWA, SUSUMU

Nationality Japanese

b 1939

*For his discovery of the genetic principle for generation of an tibody diversity*

Tonegawa moved to the Basel Institute for Immunology after he completed his Ph D at the University of California at San Diego He demonstrated that cells accomplish the gigantic task of making antibodies to order by shuffling parts of the genes that govern the production of antibodies, the cellular building blocks of the immune system The process can be likened to the rearranging of boxcars or wagons on a freight train The prevailing dogma was that the order of genes in any one person is immutable Tonegawa found thatthe "wagons" rearranged themselves in a multitude of different configurations to make the an tibodies that fight off diseases His work has led to dis coveries of how some cancers form and could help in understanding such immune disorders as AIDS or rheumatoid arthritis

1988

BLACK, SIR JAMES

Nationality British
b 1924

ELION, GERTRUDE B

Nationality American
b 1918

HITCHINGS, GEORGE H

Nationality American
b April 18 1905, Hoquiam Washington

*For their discoveries of important principles for drug treatment*

The Nobel Prize for 1988 for medicine was an uncommon break from normal tradition in that it was given to researchers in the commercial drug industry Elion and Hitchings, both Americans, are affiliated with Burrough s Wellcome in North Carolina, and the Britisher, Black, is attached to the King s College School of Medicine and Dentistry Elion and Hitchings who have collaborated since 1945, had discovered in the mid 1940 s that the genes of healthy cells process information differently from those of cancerous cells and disease-causing bacteria and viruses

They targeted these cells and microbes with drugs that interfere with replication and established an approach that resulted in new drug therapies for many diseases, like leukemia and malaria They developed the drug "azathioprine' in 1957 for controlling rejection in organ transplants This led to the development of "acyclovir" for the treatment of herpes, and AZT for AIDS

Black focussed his research on "docking ports" used by chemical messengers moving between cells He developed a drug for heart disease (1964) that blocks the effect of natural stimulants like adrenaline on special nerve receptors, or beta receptors and prevents the heart rate from increasing with damaging speed His beta blocker is widely used for treatment of hypertension and heart diseases

1989

BISHOP, J M

Nationality American

VARMUS, H E

Nationality American

*For their work with cancer genes*

Bishop and Varmus, in a series of experiments that began in the mid seventies at the University of California at San Francisco, have contributed significantly to the understanding of the mechanism of the genes, or units of heredity that cause cancer The general assumption until the startling discovery of these two scientists, was that cancer genes — oncogens — were separate entities and were not connected with the normal, healthy functioning of a cell Bishop and Varmus, by their studies on cancer-causing virus in chicken discovered that oncogens were normal genes, vital to cell development and growth In cases of cancer these genes, somehow, maybe due to mutations induced by carcinogens such as radiation and cigarette smoke, go awry

The two scientists by these findings helped explain the role of genetic damage in cancer development and established a common pathway by which all cancers seem to evolve Researchers have identified more than 40 slightly altered genes that cause cancer in humans, since then

"We have the seeds of cancer in our genetic dowry,' observed Bishop and these discoveries will make it easier for doctors to diagnose and predict the occurrence of cancer

1990

MURRAY, JOSEPH

Nationality American

THOMAS, DONNALL E

Nationality American

*For their pioneering research and contribution to tissue transplants*

Murray of Boston's Brigham and Women's Hospital, and Thomas of the Fred Hutchinson Cancer Research Centre in Seattle, Washington, shared the Nobel Prize for 1990 for their work which was crucial for those tens of thousands of severely ill patients who either can be cured or given a decent life through transplants, when other treatment methods are without success Murray and Thomas, close friends since the time of their residencies at the Brigham Hospital in the late 1940 s, had been interested in the problem of transplants for a long time

Murray became intrigued with the ideas of transplants and skin grafts during a stint as a plastic surgeon in World War II His work with thousands of burn victims got him involved in the problems of permanent skin grafting His realisation that skin grafting in identical twins worked better led him to suspect that the same may be true of internal organs After experimenting with dogs, he performed his first kidney transplants successfully between twins in 1954 and, as expected, the recipient s immune system did not reject the new organ as an invader Murray then experimented with drugs that suppressed the immune system and thus allowed transplants from close relatives and even unrelated donors

Thomas worked on leukemia, the fatal cancer of blood-forming tissues He reasoned that the replacement of the bone marrow of a patient with that of a healthy donor might arrest the disease, since blood cells are generated by bone marrow He worked on dogs, like Murray, destroying their marrow with radiation and transplanting new, healthy marrow In humans, he too found initial success with identical twins (1956) His subsequent work with immunosuppressive drugs and careful tissue matching, helped significantly to overcome transplant rejection

With the emphasis being on basic medical research this award for transplants was a rare instance of a clinical treatment receiving precedence

## 1991

**Neher Erwin**

Nationality German

b — 1944, Landsberg, Germany

**Sakmann, Bert**

Nationality German

b — 1942, Stuttgart, Germany

*For their contribution to the understanding of the cellular mechanisms underlying several diseases including diabetes and cystic fibrosis*

Erwin Neher obtained his degree in Physics from the Technical University in Munich in 1968 after which he shifted to the University of Wisconsin for his Masters degree He returned to Germany in 1972 and joined the Max Planck Institut for Biophysical Chemistry in Goettingen He has been the Director of the Institute s Division for Membrane Physics since 1988

Bert Sakmann received his medical degree from the University of Munich in 1967 A year later, he joined the Max Planck Institute for psychiatry as a research assistant From 1971 to 1973, he studied biophysics in London Upon his return to Germany, he joined Neher at the Max Planck Institute at Goettingen In 1988, Sakmann shifted to the Max Planck Institute for medicine research in Heidelberg

Neher and Sakmann's combined research conclusively established the existence of ion channels and their functions Ion channels are tunnel-like structures that let charged ion particles in and out of the cell Neher and Sakmann together developed a technique that allows the registration of these incredibly small electric currents that pass through a single ion channel. they also studied the regulation of the passage in and out of cells of positively or negatively charged ions

Their work has revolutionised modern biology, and contributed to the understanding of the cellular mechanisms underlying several diseases including diabetes and cystic fibrosis

# INDEX OF NAMES